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Ophthalmology

The Extraocular Muscles In Systemic Diseases

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It would be an understatement to say only that I appreciate the privilege of reading a paper here on this happy occasion. It is an honor to have been included on the program with distinguished colleagues, and it is deeply satisfying to visit with friends of many years.

The selection of a topic has given me concern. Presentation of something new is an impossible task for those of us who must content ourselves with using information unearthed by others. I have learned much from two remarkable texts recently published and in English. That of Adams, Denny-Brown and Pearson entitled "Diseases of Muscle" is a tremendous storehouse of information, and a smaller book by Greenfield, Shy, Alvord and Berg, "Atlas of Muscle Pathology in Neuromuscular Diseases" is extremely valuable; it contains beautiful plates, many in color. To me it is particularly valuable in that it exemplifies Dr. Greenfield's assiduity. The last lecture he gave was in the Johns Hopkins Hospital a few days before he died in Washington where he was working with his colleagues on this book on muscles. It seemed reasonable to me that a study on muscles, particularly the extraocular muscles, in systemic diseases, might hold interest for you, and that I would benefit in the preparation of such a paper. Although involvement of muscles characterizes many diseases, relatively few papers do more than draw attention to muscle palsies in affections which do not principally affect muscles. My efforts are made with realization that everything stated in this paper is available elsewhere; it may serve as a useful introduction to problems which require clarification, and these are many.

Dr. John E. Eisenlohr has helped me and I am happy to acknowledge him as co-author.

We have avoided including a table indicating a classification of diseases. The paper is admittedly incomplete, and we have been able to utilize only a small part of what is available to those who have a greater understanding of histology and pathology. It seems obvious that a principal division of material falls into two categories: (1) where the involvement of the extraocular and other striated muscles may be considered as primary, and (2) where the muscle involvement is secondary or is associated with involvement of other tissues. Actually, a majority of the affections with which we are here concerned belong to the last named group. We have not included mention of studies on muscle palsies resulting from involvement of the central nervous system above the level of the myoneural junctions. It is generally well known that changes in muscles are often difficult to evaluate, particularly when the changes are minimal. Sections from the ocular muscles are particularly likely to be difficult to assess because the sections almost invariably are small and distorted, and often contain more tendon than muscle. Finally, no effort is made here to outline present knowledge as regards anatomy, histology or physiology of striated muscle, but from time to time attention is directed to such basic considerations as they may apply to disease states.

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Inflammations

Suppurative involvements accounting for orbital abscess do not require extensive comment. Generally speaking, the involvement of the muscles is relatively slight. Possibly, this is explained on the basis of there being little muscle as compared to other tissues within the orbit. It may be that the muscle fibres are protected by the connective tissue membranes (epi-, peri, endomysium) surrounding the fibrils and the entire muscle mass, and by the sarcolemma. It is well known clinically that abscesses rarely originate in muscle, for example recall the rarity of abscess of the tongue. Adams and his colleagues have cited a more important reason than any other: muscle tissue does not provide a suitable medium for growth of many bacteria.

Gas gangrene is regularly characterized by muscle involvement. Although healthy muscle is resistant to infection by Clostridium welchii, damaged muscle is particularly susceptible (see Fig. 1). The formation of gas bubbles results from liberation of carbon dioxide in the breakdown of muscle glycogen (see Adams et al). With orbital involvement there is brawny swelling of the lids, a bloody or coffee-colored discharge, crepitation, and a foul odor with, in some instances, escape of bubbles of gas. Occasionally gas bubbles may be seen in the anterior chamber of the eye (Duke-Elder).

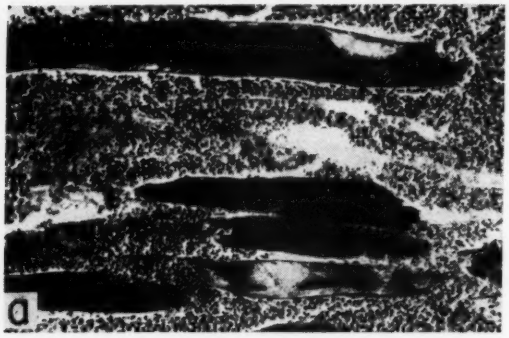

Figure 1

Gas Gangrene. Clostridial myositis. Fresh lesion showing necrotic fibres, exudation of fibrin and neutrophilic leucocytes. (Adams, Denny-Brown and Pearson, p. 288)

Tuberculosis and syphilis do not require extended descriptions. Tuberculous periostitis may account for proptosis and muscle palsies. Excepting for accidental inoculations into muscles, tuberculosis never accounts for primary muscle involvement. The resistance of muscles to tuberculous infection may be due to the high content of lactic acid in muscles (Adams et al).

Before the advent of penicillin, syphilitic periostitis was observed frequently, particularly in middle-aged Negro females according to our experience. In such cases there was absence of suppuration. Muscular involvement was evidenced by some degree of ophthalmoplegia, swelling of the eyelids, spontaneous pain and pain on palpation; positive serology established the diagnosis. Such periostitis occurred with both early and late syphilis. In those cases where ophthalmoplegia was a prominent feature the extent of the muscle involvement apart from the nerve involvement was not clear. Gummatous myositis as an isolated affection has not been supported at autopsy (Duke-Elder). However, orbital gummata have extended to involve muscles in the orbit.

Leptospirosis (Weil's disease, spirochetal jaundice) deserves mention as a systemic disease producing ocular signs: intense injection of the conjunctivae and pain on movement of the eyes. It seems probable that hemorrhages into the muscles or tissues surrounding them may be responsible for the pain. Pathological examinations have revealed hemorrhages and vacuolation, granularity and hyalinization of the sarcoplasm of the calf muscles (Adams et al; Ashe). Other ocular signs of leptospirosis are iritis and optic neuritis.

Bare mention is made of infection with a fungus, Mucoracea, characteristically observed in individuals who suffer from diabetes. We have observed cellulitis of the orbit resulting in ophthalmoplegia in a diabetic child who also exhibited evidence of extensive involvement of the meninges.

Sarcoidosis and uveoparotid fever unquestionably are one and the same disease. Sarcoidosis may involve the eyelids and orbit. The extraocular muscles may exhibit neural atrophy when the nerve is destroyed, and a localized granulomatous nodule within the muscle when it is the site of involvement. The histologic picture of "hard tubercle" so characteristic of sarcoidosis is well known; in such a lesion doubly refractile Schaumann bodies may be present. The explanation for a high serum calcium present in some cases is not clear. In such cases a band keratopathy as well as crystalline deposits in the conjunctivae may be seen. Similar ocular changes, readily visible on slit lamp examination, are sometimes seen in individuals suffering from hyperparathyroidism, vitamin D poisoning, beryllium poisoning, and when the blood calcium is elevated from prolonged milk diet. An interesting combination of diseases was observed recently by us in a male patient who suffered from carcinoma of the lung and sarcoidosis of the orbit with exophthalmos.

Pseudotumor of the orbit and orbital myositis are commented upon here because these entities well may be a local manifestation of generalized disease, although this cannot be established at this time. Ophthalmologists consider pseudotumor as a probable diagnosis when an etiology for proptosis and ophthalmoplegia is not supported by changes in the roentgenograms and when there is absence of a palpable mass in the orbit. In such cases usually there is no complaint of pain, and in a majority the visual acuity remains at normal or near-normal levels. A trial of steroid therapy is made. According to our experience pronounced improvement confirms the diagnosis of pseudotumor.

As regards ophthalmoplegia and pseudotumor, Dunnington and Berke have made a noteworthy contribution. They described cases in which myositis was the prominent feature when biopsies were made. Their patients exhibited what had been attributed to pseudotumor namely edema, diplopia and exophthalmos. The edema was variable, sometimes first involving the upper lid or the lower lid; almost invariably the involvement was unilateral. Diplopia was present almost always. Exophthalmos was variable. Ptosis, when present, was usually slight. They remarked upon the limitation of upward movement commonly being most pronounced and pointed to the value of the traction test. They emphasized the tendency to spontaneous improvement and the inadvisability of operation in such cases, but agreed that biopsy in some instances is essential to the diagnosis.

Dunnington and Berke found that all the extraocular muscles might be affected, but usually those situated inferiorly were principally involved: the inferior rectus and the inferior oblique. The muscles were greatly increased in size, and were pale, smooth and friable. The central portion of the muscles showed the principal changes. Microscopically there was fibrosis, degeneration and collections of lymphocytes. They pointed out that

such changes were precisely what is observed in the muscles of patients suffering from malignant exophthalmos associated with thyroid involvement. They predicted that future investigations might show that orbital myositis is the primary lesion in malignant exophthalmos.

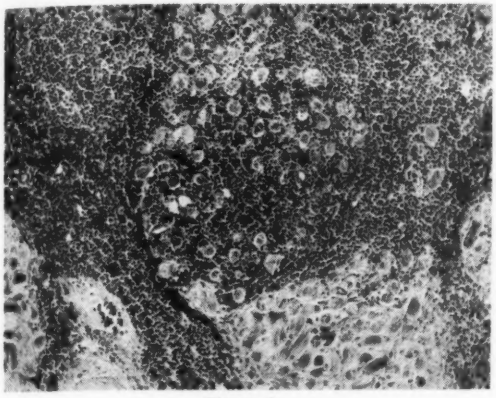

Figure 2

Section of extraocular muscle from a patient with marked exophthalmos on the left which failed to respond to steroids. The inferior rectus was particularly involved. There is diffuse infiltration with lymphocytes and plasma cells with slight atrophy of muscle fibers. There is no mention of thyroid studies having been done. The opposite eye became involved a year later with the same process, and responded encouragingly to steroids x 130. (AFIP Acc. No. 824224)

Figure 3

Orbital myositis. Note that the right eye is pulled downward by involvement of the muscles in the lower part of the orbit. The eye could not be elevated by traction with forceps. (Walsh, 2nd Ed., p. 962)

Parasitic Involvement of the Extraocular Muscles

Several parasites may invade the orbit and the eye but a selective affinity for invasion of the extraocular muscles is seen only with trichiniasis, so far as we are aware. It has been estimated that one of six inhabitants of the United States harbors Trichinae; each year 350,000 individuals acquire the infection and of these 16,000 develop symptoms; an estimated 5 per cent of these die (Greenstein and Steinberg).

Before considering trichiniasis and its ocular symptomatology mention is made of the frequency of Echinococcus infestation in Manitoba during the early 1900's. We surmise that such a finding nowadays would be unique. Also it is of interest that parasites, particularly Onchoceriasis, are second only to trachoma as blinding agents throughout the world. In many instances in North America parasites, nematodes and the protozoan toxoplasma, are responsible for endophthalmitis. It is of interest that with such parasitic involvements completely conclusive proof of etiology can frequently be produced by identification of organisms, and this cannot be said regarding ocular involvements attributed to tuberculosis and syphilis in a vast majority of cases.

Trichiniasis results from invasion of body tissues by larvae of Trichinella spiralis about eight days after ingestion, and at this time the muscles are painful to touch and eye movements cause pain. Usually the eye signs are predominant; chemosis of the bulbar conjunctivae with a lemon-yellow appearance. Edema of the eyelids may be extreme and it often extends to the face. Ophthalmoplegia is present in variable proportions. Optic neuritis, retinal hemorrhages and exudates have been observed. The diagnosis is made on the history of eating pork, eosinophilia, and positive test to Trichina antigen. The mortality is high in severe cases in young children, but is low in adults. In late cases roentgenograms show calcified cyst walls in the muscles, and we have observed these shadows in x-rays of the skull. Recently Greenstein and Steinberg found ACTH to be effective in treating three children in whom the diagnosis was established by biopsy (cysts in the gastrocnemii after recovery). The mechanism through which ACTH is effective is not presently understood.

Only recently a report has been made on Cysticercus cellulosae involving an ocular muscle (Nirankari).

Metabolic Diseases and the Extraocular Muscles

Thyroid disorders are associated with changes in the extraocular muscles, and one of the principal eye signs of thyroid disease is exophthalmos. We accept the concept that certain of these cases of exophthalmos are properly described as thyrotoxic and others as thyrotropic in origin. This is a convenient clinical distinction by no means always possible of application. We are omitting discussion

of relationships which are thought to exist between thyroid and pituitary activities. The ocular signs which require explanations here are lid signs (lid-lag and retraction), exophthalmos and ophthalmoplegia. Comment on each of these is made after we have described changes in the extraocular muscles.

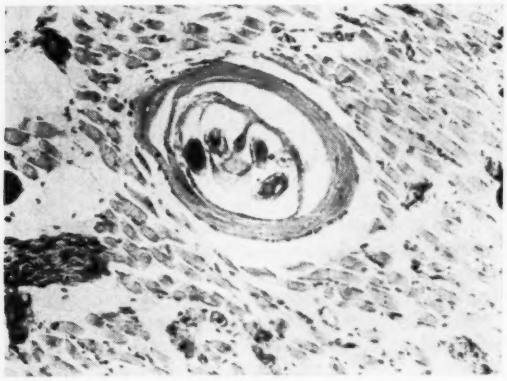

Figure 4

Trichiniasis. Encysted larva in ocular muscle. (Wilmer Institute Pathology Laboratory)

Figure 5

Malignant exophthalmos. Orbital decompression effective. Vision on admission perception of light bilateral, total ophthalmoplegia, exudates in anterior chambers. Thyroidectomy had been done a year before exophthalmos became severe. Final vision 20/40 for each eye. (Walsh, 2nd ed., p. 685)

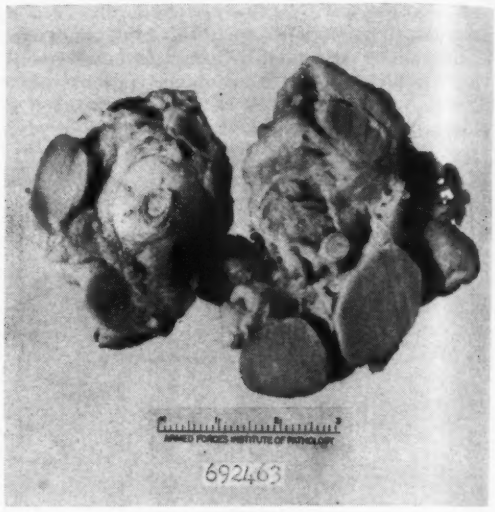

Figure 6

Gross specimen from a 65 year old white female with progressive thyrotropic exophthalmos showing marked enlargement of particularly the medial and inferior recti and the inferior oblique. (AFIP Acc. No. 692463)

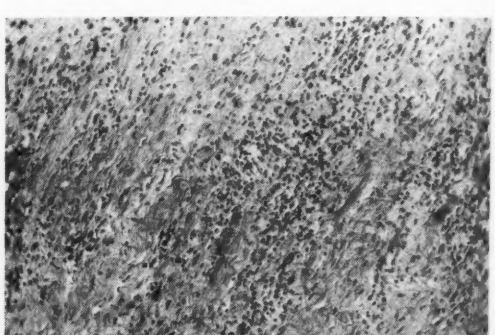

Figure 7

Microscopic view of the specimen shown in Fig. showing far advanced degeneration of the muscle fibers with the bulk of the tissue formed by dense hyalinized connective tissue. There is a diffuse infiltration of plasma cells and other mesenchymal cells x 145. (AFIP Acc. No. 692463)

Increased size of the ocular muscles is observed in progressive or so-called malignant exophthalmos (see Fig. 6). The muscles may become several times normal size. The enlargement is principally central so that they become fusiform. They are pale and rubbery to touch. Edema is largely responsible for the increase in size. Lymphocytic infiltrations which vary from case to case in part may explain the increased size. Fibrosis is present in variable proportions; seemingly it is a replacement process. Fibrosis tends to be irregular hence a single section may not reveal it. It may prevent recession of a proptosed eye after subsidence of the acute phase of the progressive disease. Why the edema and lymphocytic infiltration occurs is not thoroughly understood (see Fig. 8). Both could be due to hormonal influences. What the blood supply to the orbit and the orbital muscles within it has to do with increased volume of orbital contents has not been established. It has been suggested that increased size of orbital structures may result in venous compression, and that this in turn establishes a vicious circle. Also it has been shown that there is an increase in mucin content of muscles in

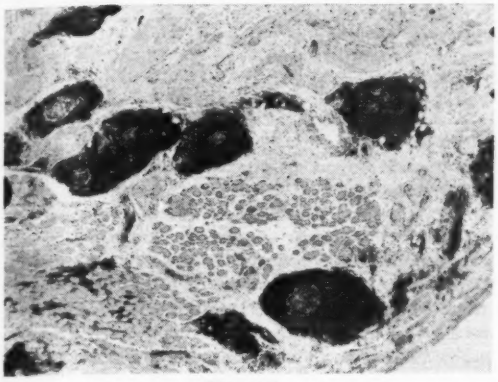

Figure 8

Extraocular muscle in thyrotropic exophthalmos. H. and E. x 40. (Wilmer Pathology Laboratory). Note follicle formation, lymphocytes 30972.

experimental and clinical exophthalmos, and that a temporary decrease in exophthalmos has followed the injection of hyaluronidase (Wybar).

Up to this time we have considered increased size of muscles associated with thyroid disease. There are abnormal thyroid states in which the muscles are essentially normal sized or smaller than normal. Generally speaking when the muscles are normal or smaller than normal in the presence of exophthalmos the case falls into the category of thyrotoxic disease. Atrophy may account for the diminished size of the ocular muscles. Adams, Denny-Brown and Pearson remarked upon the relative infrequency with which the ocular muscles of thyrotoxic patients have been examined. They pointed to interesting changes in such muscles, a lipomatosis with rows of fat cells infiltrating between the muscle bundles and at times between individual fibres (see Fig. 9). Also they remarked on increased fat content of other orbital tissues, atrophy of muscle fibres accounting for a decreased over-all diameter, and to formation of granular clumps resembling giant cells within the muscles. Rundle and Pochin found the fat in the eye muscles to be twice normal in a group of seventeen individuals with thyrotoxicosis. The fat deposition was greatest in the levator muscle. The orbital tissues, particularly fat, are hydrophilic to a greater degree than is the muscle. That orbital tissues and particularly orbital fat have an affinity for water uptake is shown by an experiment in which such fat transplanted into the orbit of an experimental animal had a greater power to absorb water than had transplanted fat from another site (Wybar).

From what has been stated it becomes obvious that with progressive exophthalmos of the malignant variety increased size is the remarkable change in the extraocular muscles. With thyrotoxic exophthalmos increased fat content of the muscles and of the other tissues is a principal factor explaining the exophthalmos. Considering the

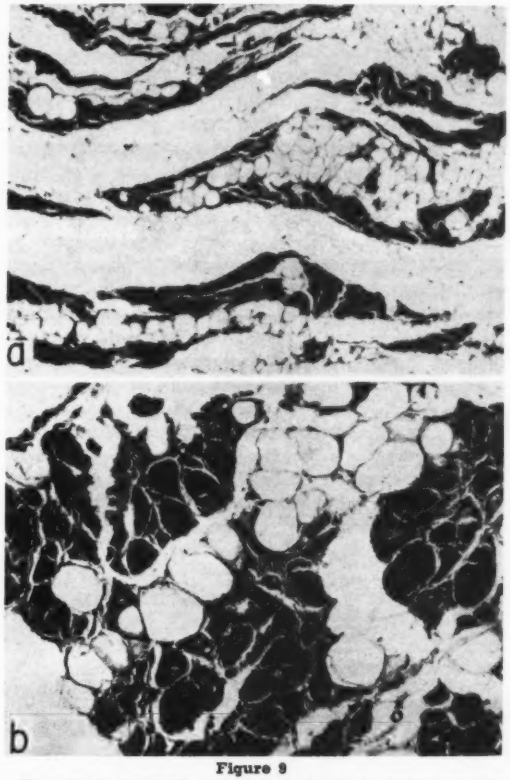

Figure 9

Thyrotoxic myopathy. Lipomatosis of an ocular muscle in a fatal case of hyperthyroidism (from Adams, Denny-Brown and Pearson, p. 469).

loss of weight associated with thyrotoxicosis increase in orbital fat seems anomalous. Whereas the clinical picture of thyrotoxicosis may be changed to apparent normalcy by thyroidectomy we do not know in humans that the changes in the muscles are reversed.

Acute thyrotoxic myopathy and acute toxic encephalomyopathy are characterized by muscular weakness, and in particular the bulbar muscles are affected. In fatal cases there is delirium, coma and death. Thyrotoxic myopathy may represent a combination of myasthenia gravis and hyperthyroidism, as is described later in this communication.

Lid Signs

Retraction of the upper eyelids and lid-lag (von Graefe's sign) require comment and are considered together. It has been proposed that the sympathetic innervation of the upper lid is responsible for both these signs. In this regard it has been observed that there is absence of change in the position of the lower eyelid when the upper lid is retracted. Usually the pupil is not dilated. Consequently it seems doubtful that sympathetic innervation is responsible for the lid retraction. It has been suggested by Meadows that lid retraction is due to

spasm of the levator. Possibly the increased fat content in the levator is responsible. A levator spasm would seem a reasonable explanation for lid-lag. That lid retraction is truly part of the hyperthyroidism seems undoubtable because it disappears with recovery from thyrotoxic symptoms. Brain describes a case which supports the viewpoint that sympathetic overaction is not responsible for lid retraction associated with thyrotoxicosis. His patient suffered from syringomyelia and thyrotoxicosis. On the right the pupil was smaller than the left but both were small and both upper eyelids were retracted. After effective medical treatment the upper right eyelid was slightly ptosed, the left assumed a normal position (see Fig. 10). We have seen unilateral or bilateral lid retraction notably in young individuals when all other findings including laboratory tests were normal. Invariably such individuals ultimately developed evidence of thyrotoxicosis.

Figure 10

Patient had bilateral retraction of upper eyelids. Suffered from syringomyelia accounting for small pupil on the right. After thyrotoxicosis had yieldel to therapy the right eyelid was slightly ptosed, the left in normal position (from Brain, W. R. in Lancet, 1939, 2: 1217).

Exophthalmos

Exophthalmos requires further comment. Often it is impossible to state with assurance whether a case of exophthalmos falls into the thyrotoxic or thyrotropic category. An individual with thyrotoxic exophthalmos may develop thyrotropic exophthalmos later when the basal metabolic rate and iodine uptake are normal or approximately so. As regards malignant exophthalmos lateral decompression of the orbit has sufficed in most cases in our experience. With thyrotoxicosis, thyroidectomy seems to improve the exophthalmos, but the improvement is more apparent than real; narrowing of the lid fissure responsible for the improved appearance (Soley).

Ophthalmoplegia

With thyroid disease ophthalmoplegia is present on the basis of changes in the muscles rather than as the result of nerve palsies. With thyrotoxicosis with or without exophthalmos some evidence of muscle weakness is present in a high proportion of cases. Generally speaking it seems that the severity of the ophthalmoplegia is in inverse proportion to the degree of thyrotoxicity, as stated by Meadows. This observation is of importance in selection of cases for thyroidectomy. It is not advisable to operate when there is excess edema and pronounced ophthalmoplegia in an individual with relatively mild thyrotoxicosis. Persistence of some degree of ophthalmoplegia with thyroid disease properly treated is readily understood on the basis of fibrosis within the muscles.

Hypothyroidism

Hypothyroidism is characterized by edema of the eyelids which in some cases amounts to an elephantiasis. There is hypertrophy of subcutaneous tissues, increase in thickness of blood and lymph vessels, and the epidermis may become atrophic. There may be development of hyperkeratoses. In some instances there is development of exophthalmos for which thyrotropic hormone may be responsible. The extraocular muscles are not affected either in cretins or in individuals with acquired hypothyroidism, according to our experience. However, there are changes in the skeletal musculature which are remarkable. In children the syndrome of Debre-Semelaigne includes enlargement of the muscles, weakness and ready fatiguability. In adults this is known as Hoffman's syndrome. Movements may be slow and simulate myotonia.

Hypothyroidism and Myotonia

In some instances hypothyroidism is associated with myotonia. Goldstone and Ford have described this in individuals who after thyroidectomy developed evidences of thyroid insufficiency and myotonia. Their paper includes pertinent references. We have seen a patient whose case they reported. Briefly, this woman underwent thyroidectomy and subsequently developed evidence of thyroid insufficiency and myotonia. The myotonia was severe; she had to "fall" into a chair and could not arise without help; her hand grasp was classically that of a myotonic. When she closed her eyes on request she was unable to open them for a few moments. The eyes did not move immediately on request but the movements were full; there was occasional internal strabismus which was fleeting. When Doctor Ford first saw this patient the ocular defects were not noted. She responded to thyroid medication, and was completely free of symptoms for years. Through the courtesy of Doctor Ford we saw her after she had greatly reduced her thyroid intake. Coincident with this she again developed myotonia and the ocular involvement already mentioned. When the intake of thyroid was increased she made a complete recovery.

Von Gierke's Disease

Von Gierke's Disease deserves mention, although in the few patients with this disorder that have come to our attention there have not been any ocular signs of interest. The disease is a rare, congenital and sometimes familial disorder in which there is an accumulation of glycogen in various tissues chiefly the heart and liver (Ford). There is profound muscular weakness and loss of tone which simulates amyotonia congenita.

Diseases Seemingly Dependent Upon Changes at the Myoneural Junctions

Myasthenia gravis has been described as a chemical disease on the basis of the efficacy of cholinergic substances, such as prostigmine, in therapy. The concept is that circulating cholinesterases are responsible for the symptomatology, and that prostigmine as an anticholinesterase allows available acetylcholine to function. In many instances there are minimal changes in the extraocular muscles. In some there are collections of lymphocytes known as "lymphorrhages;" these are found in the vicinity of blood vessels. There are no changes in muscle fibers adjacent to the accumulation of lymphocytes (Adams et al). In some instances there is profound atrophy of muscle fibers as we have observed in a single fatal case (see Fig. 11). Lymphorrhages occur in other affections of muscles. Greenfield and his associates listed from their case studies: dystrophia myotonica, neurasthenia, flabby infant, scleroderma, amyotrophic lateral sclerosis and a case of sensory-motor neuropathy. Lymphocytic infiltrations have already been mentioned as occurring in cases of thyroid and post-hyperthyroid exophthalmos.

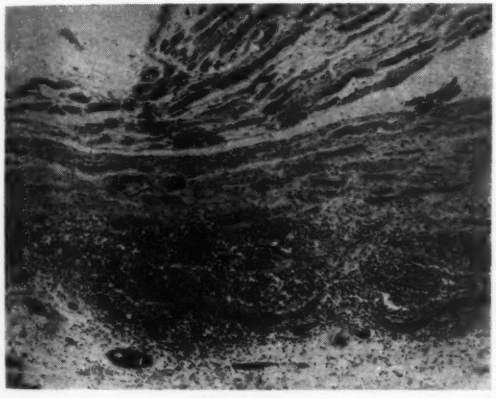

Figure 11

Section of ocular muscle from a fatal case of myasthenia gravis showing marked atrophy of the muscle tissue, a dense focal collection of lymphocytes-a lymphorrhage. No thymus gland was found at autopsy x 86. (AFIP Acc. No. 677734)

Myasthenia gravis may be observed in individuals who suffer from thyrotoxicosis. We have observed a woman who exhibited evidences of ocular myasthenia gravis and hyperthyroidism. As a result of thyroidectomy there was a remission of the myasthenia and this has persisted for several years. Meadows has not observed a favorable response to thyroidectomy in such cases.

Myasthenia gravis is frequently encountered. Usually it occurs during early or middle life. It is extremely rare as a congenital and persistent disorder. Levin has described congenital cases. We have recently diagnosed myasthenia gravis in three boys in a family. All have had some ptosis and ophthalmoplegia throughout their lives. The oldest boy now seventeen years of age has been confined to a wheel-chair for years. This boy requires medication constantly in order to continue his work as a student. In all there was a pronounced response to prostigmine. The severely affected boy changes his position like a patient with muscular dystrophy. This family is being reported elsewhere by Dr. William F. Hoyt and by one of us. Walton, Geschwind and Simpson reported the case of a woman who was always excessively weak after exertion; she responded favorably to prostigmine but not to tensilon. They suggested that their patient belonged to a borderland between myasthenia and primary myopathy, and stated that a biopsy of a muscle showed changes compatible with myopathy. Occasionally myasthenia gravis is observed as a transistory phenomenon in the infant of a mother who is suffering from the disease. Such an infant cannot suckle or cry properly and responds immediately to a small amount of prostigmin injection (1/50 mgm). Such dosage repeated every three or four hours suffices for approximately two weeks when it becomes obvious that symptoms of prostigmin poisoning are appearing. Thereafter no treatment is necessary. Seemingly, circulating cholinesterases from the mother's blood are responsible for the infant's myasthenia. When the maternal influences have been eliminated the evidence of the disease disappears in the infant.

Just as prostigmin and tensilon are valuable in the diagnosis and treatment of myasthenia gravis, quinine is harmful and may excite an exacerbation of the disease. Curare is occasionally used in diagnosis in doubtful cases by increasing the muscle deficiency which then can be controlled with prostigmin. Curare is rarely necessary in diagnosis and can be dangerous.

Some interesting features regarding myasthenia gravis, particularly ocular myasthenia gravis, are mentioned. The diagnosis of myasthenia gravis is missed for a time, when it is thought that hemorrhage in or tumor of the brain stem exists (see Fig. 12). Another example of misdiagnosis of brain stem involvement was seen in a 23-year old man who developed diplopia the day after he had been thrown forcibly against the steering wheel of his car. Possibly he had triggered the myasthenia by trauma to the thymus gland which, however, should have been atrophic. Retraction of one upper eyelid is explained on the basis of secondary deviation when the other lid is ptosed. Exophthalmos has been described as a rare manifestation of ocular myasthenia gravis. If such exophthalmos is truly present, it may be due to coexistent thyroid disease. As regards exophthalmos and lid retraction responding to prostigmin, as described by Hatch, we do not have a satisfactory explanation. It is valuable to know that, when myasthenia gravis has affected only the ocular muscles for as

long as two years, there is little likelihood of the involvement becoming generalized, as has been pointed out by Harvey and Grob. Electromyography gives a classical picture with myasthenia gravis, but it is rarely necessary to the diagnosis. Finally, it is a good rule to follow that given a patient with ophthalmoplegia when the etiology is not obvious, and when the pupillary responses are normal, a diagnostic injection of prostigmin or tensilon may produce the diagnosis. Furthermore, it is to be recalled that elevation of a ptosed eyelid as the result of such an injection is easier to assess than an increase in movements of the eyes.

Figure 12

Myasthenia gravis simulating bilateral anterior internuclear paralysis (Walsh, Clinical Neuro-ophthalmology, 2nd ed., p. 781)

Figure 13

Myasthenia gravis. Pictures on left before administration of prostigmine, pictures on right after injection (from Hatch, H. A., New England J. Med., 1952, 246: 856).

Family Periodic Paralysis

This curious familial disease, characterized by recurrent attacks of flaccid paralysis of striated muscles, loss of tendon jerks and loss of electrical reactions, is relieved by the administration of potassium. Examination of the muscles in these cases has not shown anything abnormal. We have observed ocular signs in only a single case. There was bilateral ptosis and some degree of limitation of ocular movements. It is of interest that Donald McEachern noted the frequency of hyperthyroidism and goiter in a series of cases reported by Shinosaki and Tusji.

Tetanus

Tetanus has been generally considered as a central nervous system disease. However, when one considers the muscular contractions which persist unabated for weeks in the absence of convulsions, it seems there must be a mechanism within the muscles which account for the contraction. Abel pointed out that local tetanus can be explained on the basis of direct involvement of nerves, but that the generalized disease is dependent upon a toxin circulating in the blood. Seemingly, this toxin affects the myoneural junctions hence the constant spasm as seen in the muscles of the face. Facial palsy in such cases probably is always or nearly always a misdiagnosis. As regards the eyes, ophthalmoplegia could be similarly explained.

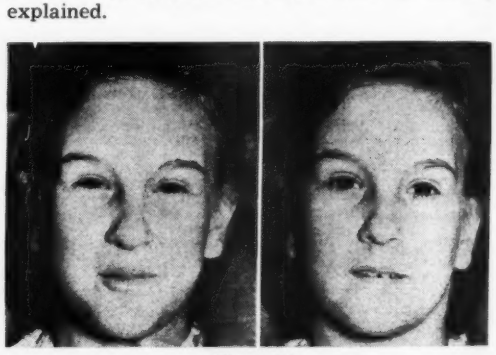

Figure 14

Facial tetanus; risus sardonicus. Picture on right taken two weeks after that on left. Abdominal muscles remained rigid for weeks. (Walsh, 2nd ed., p. 724)

Botulism

Botulism is another disease in which, in all probability the palsies are explained on the basis of toxins influencing the muscles at the myoneural junctions. It is of course well known that hemorrhages occur in the brain stem and in the cord, but there is good evidence that the signs result from peripheral rather than from central involvement. Adams et al stated that cholinergic motor fibers are affected by appropriate dosage of the toxin of clostridium botulinum. When the muscles are paralyzed they fail to respond to stimulation of the motor nerve but do respond to intra-arterial acetylcholine injection. In animals given the toxin the motor nerves conduct impulses normally and the individual muscles react to direct stimulation therefore the block must be between the nerve and the muscle.

Involvements of the ocular muscles are the first evidence of botulism. There is ptosis, diplopia, limitation of movements, nystagmus and some degree of internal ophthalmoplegia.

Degenerative Disease and the Extraocular Muscles

Many affections which may produce changes in the muscles are not considered here, since their influences are at a higher level than the myoneural junctions. Some such conditions are: myotonia congenita, polyneuritis, diphtheritic paralysis, amyotrophic lateral sclerosis, disseminated sclerosis.

Myotonia Congenita

This disorder, which usually is transmitted as a dominant trait, is characterized by hypertrophy of muscles which seem weaker than normal; the seeming weakness may be due to inability to relax antagonistic muscles. The affection makes its appearance during early life. Often there is some degree of mental deficiency. All the striated muscles may be affected. Involvements of muscles of the tongue may account for difficulty in nursing. The muscles of the arms and legs are usually particularly affected. The hand grasp cannot be relaxed quickly. sudden closure of the eyelids may be followed by inability to open the eyes for several seconds. Transient squints may be observed. Cold weather increases the myotonia.

The only demonstrable change in the muscles is hypertrophy.

Creatine tolerance is increased in individuals exhibiting myotonia congenita and it is decreased in those suffering from myotonia dystrophica (myotonic atrophy). Quinine or ionized calcium is of great value in depressing the myotonia of individuals who suffer from myotonia congenita or myotonia dystrophica. Potassium and acetylcholine excite contractions of muscles and consequently increase myotonia in both of these diseases. Quinine is of value because it lengthens the refractory phase of excitable tissues. Curare does not eliminate the development of myotonia on percussion. It seems probable that myotonia congenita and myotonia dystrophica do not arise as a result of changes at the myoneural junctions as seems to be established with myasthenia gravis. If the myoneural junctions were the principal sites explaining the myotonia, curare should eliminate the sensitivity of the muscles to percussion. Probably quinine, potassium, also prostigmin influence the muscles beyond the myoneural junctions.

It is interesting and remarkable that congenital myotonia or something closely resembling Thomsen's disease in humans has been described in a strain of goats variously described as "nervous," "stiff-legged" or "fainting goats." Kolb described the syndrome, as he observed it in four goats (see Fig. 15). "From the description given by previous observers one learns that, when the goats are startled and make an effort to run away, they sud-

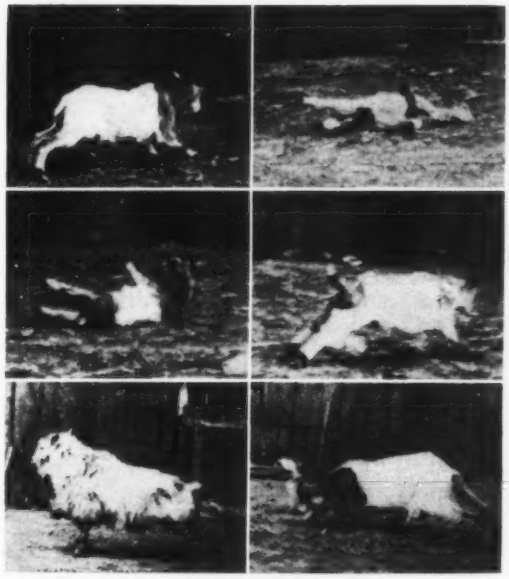

Figure 15
Goats exhibiting congenital myotonia (Kolb, L. C., Bull Johns Hopkins Hospital. 1938, 63: 221).

denly become rigid in all four extremities, and are unable to move. Thus affected they may remain motionless in a standing position, with rigidly extended legs, for a period of ten to twenty seconds. An animal caught off its balance by the seizure may fall to the ground with the four extremities fixed in extension. After a little while he is able to regain a standing position, but if he attempts to run off immediately, his hind legs may remain stiff for the first few successive leaps. During this time the limbs can be moved passively only with difficulty, but once the stiffness has subsided, the animals are entirely free from symptoms for a period of twenty to thirty minutes, after which another attack may be induced. The seizure is not accompanied by loss of consciousness or by clonic movements of the extremities and there is no evidence of autonomic nervous disability. In less severe attacks the muscular rigidity may persist only for an instant, or the animal may do no more than drag its hind legs for a few steps. In almost all cases, however, the animal becomes too stiff to jump over objects a half to one foot in height. It is said that during the attacks the diaphragm may become fixed, causing respiration to cease for a few seconds. Isolated reports of animals dying in severe attacks have not been confirmed by any writers upon this subject." (Kolb). Kolb studied a billy and nanny goat. During pregnancy the nanny goat exhibited no tendency to myotonia, and it could not be induced in her until a month after pregnancy terminated. The kids were asymptomatic until they were one month old. The reactions

of the myotonic goats to quinine and to prostigmin were the same as those produced in individuals suffering from myotonia congenita.

Myotonic Dystrophy (Myotonic Atrophy)

This is an heredofamilial disease which is more severe than myotonia congenita. It is characterized by a selective atrophy of muscles, myotonia, and other dystrophic signs (baldness, atrophy of gonads, premature senility, mental deficiency). It is seen more often than myotonia congenita and in it the muscles show characteristic changes. Individuals with myotonic dystrophy respond favorably to quinine and unfavorably to prostigmin. The ocular signs are ptosis and cataracts. Myotonia in this affection is said to affect the pupil but we have not seen this.

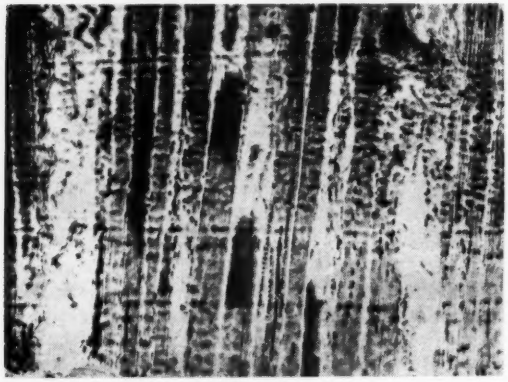

Figure 16

Myotonic dsytrophy. Note chains of sarcolemma nuclei. (Gifford, S. R., Bennett, A. E. and Fairchild, N. M.) (Arch. Ophth. 1929, 1: 335

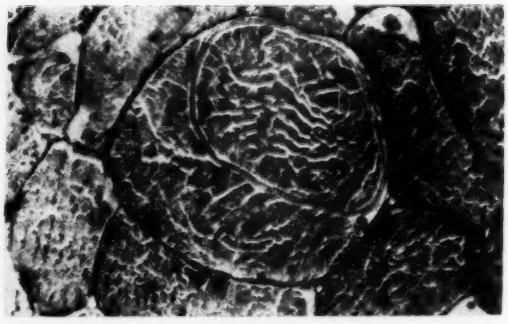

Figure 17

Myotonic dystrophy. Muscle fiber in cross-section with eccentrically placed ring fibril. Sarcoplasmic masses, ringed fibers and internal nuclei tending to be in chains are seen in this disease (from Greenfield, J. G., Shy, G. M., Alvord, E. C. and Berg, L., p. 34)

Progressive Muscular Dystrophy

Pseudohypertrophic muscular paralysis is a principal type of muscular involvement not associated with central nervous system changes. We have not seen any example of ocular muscle involvement in association with this disease. It is characteristic that the muscles of the hands and face are spared until late in the disease.

Progressive Dystrophic Ophthalmoplegia (Primary Ocular Myopathy)

Until recently it has been generally accepted that such ophthalmoplegias have resulted from a selective degeneration of the nuclei of the nerves supplying the extraocular muscles. Such cases have been regularly described as "progressive nuclear ophthalmoplegia." Sparing of the pupil is invariably a feature. Usually the first evidence is ptosis; this is followed later by limitation of ocular movements which progresses until finally the eyes are quite immobile and are slightly divergent. In some instances movements of the eyes are restricted before ptosis appears. We have observed a father who had ptosis and total immobility of the eyes; his daughter and son exhibited total immobility of the eyes, but not ptosis. When ptosis is present there also is weakness of closure of the lids.

Kiloh and Nevin suggested that in all probability nuclear involvement does not explain the syndrome of progressive external ophthalmoplegia which usually is familial. They termed the affection "progressive dystrophic ophthalmoplegia." They based their conclusion on two points: (1) progressive ophthalmoplegia externa seems related clinically and pathologically to the Landouzy-Déjérine type of muscular dystrophy which Adams and his colleagues described as a mild muscular dystrophy restricted to the facio-scapular-humeral muscles. Certainly in some instances what commences as a purely ocular muscle involvement extends to involve the muscles of the face and shoulder girdle. (2) Autopsied cases of so-called "progressive nuclear ophthalmoplegia" revealed only a few changes in the nuclei, not more than would be anticipated as secondary to failure of the muscles to function. Since the concept of Kiloh and Nevin became known to us it has seemed a reasonable explanation for most cases of progressive external ophthalmoplegia, particularly in view of the fact that pupillary sparing is invariable (see Figs. 18, 19).

Because retinitis pigmentosa is properly considered to be a degenerative disease with principal pathologic changes in the retina, and because retinitis pigmentosa may be associated with ophthalmoplegia, it might seem reasonable that the ophthalmoplegia originated in central nervous system changes. However, with such cases in our experience there has always been pupillary sparing, and this suggested that the ophthalmoplegia might result from changes in the ocular muscles. Kearns and Sayre recently have shown proof of this. In a patient who exhibited retinitis pigmentosa and ophthalmoplegia death occurred as a result of heart block. Examination of the central nervous system failed to reveal changes in the nuclei of

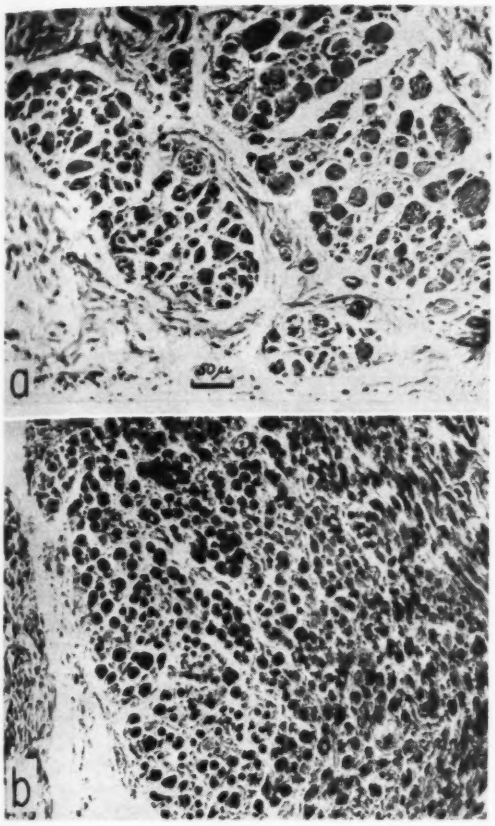

Figure 18

(a) Section of ocular muscle from case of progressive dystrophic ophthalmoplegia.

(b) normal muscle, same magnification.

Note particularly the variability in size of muscle fibers, some larger than normal and others smaller (from Nevin as reproduced in Adams, Denny-Brown and Pearson, p. 272).

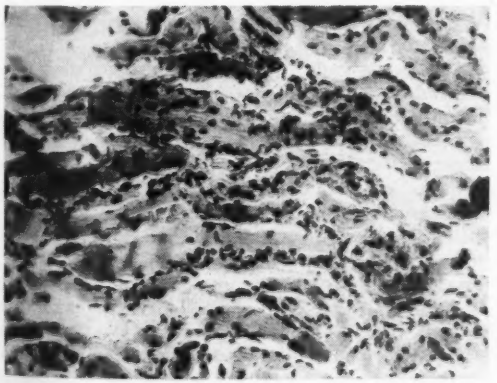

Figure 19

Medial rectus muscle in ocular myopathy, H. and E. x 200 (Wilmer Pathological Laboratory).

the nerves to the ocular muscles, and the extraocular muscles showed changes compatible with dystrophic myopathy. Two other recent papers require mention. Kornzweig and Bassen, also Jampel and Falls have described retinitis pigmentosa, acanthrocytosis and heredodegenerative neuromuscular disease. These three papers exemplify what might be described as a symbiosis of disease states as evidenced by retinal, muscular and blood changes.

Although not to be considered as systemic disease, brief mention is made here of two congenital syndromes involving extraocular muscles, Duane's and Moebius' syndromes. In the first of these, the retraction (Duane's) syndrome, in most instances there are two principal features, failure of abduction of the affected eye, and retraction of that eye when it is adducted. Because of the abduction defect many such cases have been attributed to sixth nerve paralysis. In a majority the defect is explained by fibrotic changes within the muscle. Moebius' syndrome has been attributed to failure of development of the sixth and seventh nerve nuclei, and in some instances there is an aplasia of these nuclei. However, it is probable that in many such cases the defect is in the muscles and not in the nerve nuclei. As pointed out years ago by Dr. Frank R. Ford, with Moebius' syndrome there is absence of facial sagging as would be anticipated with a neurogenic involvement, and furthermore the muscles of the face are firm on palpation.

Amyloidosis

This is a disease which may produce changes in muscles including the ocular muscles. Its etiology is unknown. In it there is deposition of amyloid (a protein-chondroitin-sulphuric acid complex (Gutman) in various body tissues. It is customary to consider amyloidosis as primary or secondary; they may be related or may merge one with the other (Adams et al). Secondary amyloidosis may be associated with chronic suppurative disease, rheumatoid arthritis, tuberculosis, multiple myeloma; it involves principally the spleen, liver and kidneys. In the secondary form involvements of the peripheral nerves and muscles are rare, but such are common in the primary form of the disease (see Fig. 20).

Primary amyloidosis is a rare disease according to reported cases. Ophthalmologists have recently become aware of its importance notably as the result of Andrade's report and more recently from an excellent study by Falls et al. The disease may manifest itself by the development of a solitary tumor or multiple tumors likely to involve the tongue or larynx. It may be widely distributed. Handousa reported on a unilateral exophthalmos resulting from a mass of amyloid in the orbit; he attributed it to chronic inflammation, but it possibly could have been primary amyloidosis.

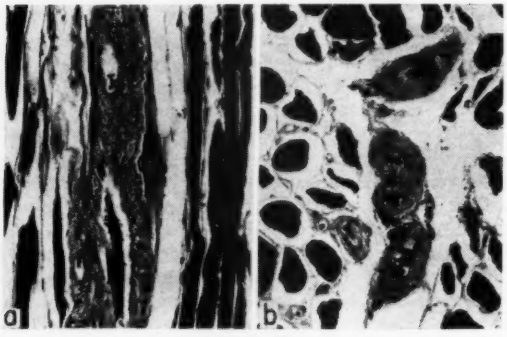

Figure 20

Amyloid disease. Skeletal muscle stained by periodic-acid Schiff method. The amyloid is stained black in the perimysial connective tissue and the walls of intramuscular blood muscles. (From Adams, Denny-Brown, and Pearson, 464)

Andrade's summary of the essential symptomatology was (1) progressive lowering of the general state of health, (2) gastrointestinal disturbances, (3) premature impotence, (4) impaired sensation in the lower extremities with muscular fibrillations, diminution and later loss of ankle jerks, (5) disorders of sphincters, (6) trophic lesions, (7) pupillary disorders. We have observed a thirty-two year old woman in whom tabes dorsalis was suspected because of internal ophthalmoplegia and loss of reflexes; spinal fluid protein was 338 mg. per cent; serologic tests on blood and spinal fluid were negative. It was learned that the patient's brother who had been hospitalized elsewhere was thought to have tabes, but he had had a goiter removed and amyloidosis was diagnosed on the basis of histologic study of the thyroid gland. Our patient obviously had familial primary amyloidosis. There are reports available concerning amyloid disease and peripheral neuropathy, and Adams and his colleagues have suggested that amyloid disease may be responsible for some of the peripheral neuritides associated with diabetes.

Falls and his associates stated that their study of 154 recorded cases of primary hereditary systemic amyloidosis suggests "that this unusual entity bids to replace syphilis as the great mimic." They remarked on the presence of retinal periarteritis with or without sheet-like vitreous opacities as suggestive of amyloidosis to the ophthalmologist in any patient with bizarre and unexplained widespread symptomatology. They remarked on change in the electrophoretic pattern of the serum lipoproteins as helpful in the diagnosis.

The Collagen Diseases and the Extraocular Muscles

Diseases which are characterized by collagen degeneration in connective tissue include dermatomyositis periarteritis nodosa, erythema multiforme, rheumatoid arthritis and scleromalacia perforans. Although each of these affections may be associated with ocular signs attention is directed here only to dermatomyositis which is of particular interest as regards ophthalmoplegia and differential diagnosis.

Dermatomyositis, Neuromyositis

These terms indicate a combination of inflammatory involvements of the skin and muscle, or of nerves and muscle. If only muscle is involved the affection is termed polymyositis. Two types of polymyositis are distinguished: the "acute" type which has a self-limited course, and chronic polymyositis which is progressive; symmetrical weakness, tenderness and induration of muscles occurs in all types (Adams et al). The affected muscles show infiltration with inflammatory cells, degeneration and replacement with fibrous tissue if the process has been of long duration (see Fig. 21).

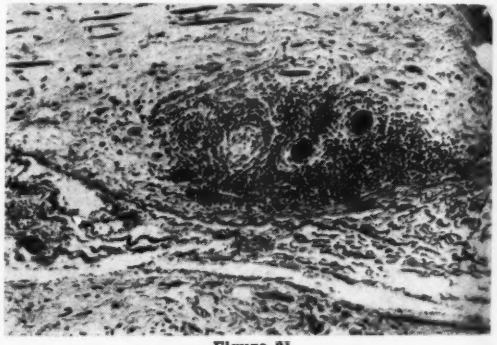

Figure 21

Dermatomyositis. Nodular collection of leucocytes, mostly lymphocytes, arranged about vessels (from Greenfield, Shy, Alvord and Berg, p. 54).

Acute dermatomyositis with which we are familiar, has occurred in children most often. At the onset there is pain over the affected muscles and there may be increased temperature and leucocytosis or eosinophilia. In most cases the muscles of the shoulder girdle, upper arms and thighs are first affected. The skin over the affected muscles may be reddened or white and thickened. The jaw muscles are frequently affected and there is difficulty in swallowing. Scleroderma may be associated.

As regards ocular symptomatology and diagnosis, the reddening of the skin may suggest erysipelas. In cases in which the skin of the brow is thickened and white the appearance is described as "marble brow." Because of the eosinophilia in some cases with reddening about the eye trichiniasis is suspect; furthermore both in trichiniasis and dermatomyositis x-rays may show calcareous deposits in the muscles late in the course of the disease. Dermatomyositis in producing difficulty in swallowing may be confused with myasthenia gravis because in both diseases regurgitation through the nose is often described. In addition to oculomotor palsies other ocular signs are: conjunctivitis, iritis and a retinitis indistinguishable from that seen in some cases of lupus erythematosus.

Temporal Arteritis

Involvement of the extraocular muscles in temporal arteritis is not a prominent feature of the disease. Wagener and Hollenhorst in a study of 122 individuals suffering from this disease remarked on a history of diplopia in twelve cases, but they found at examination only three examples of extraocular muscle involvement. They remarked upon the variability of the muscle weaknesses, and the similarity of these to the involvement of the jaw muscles. Intermittent claudication of the jaw rather often is a feature of the disease. In temporal arteritis the characteristic feature is perivascular giant cell arteritis.

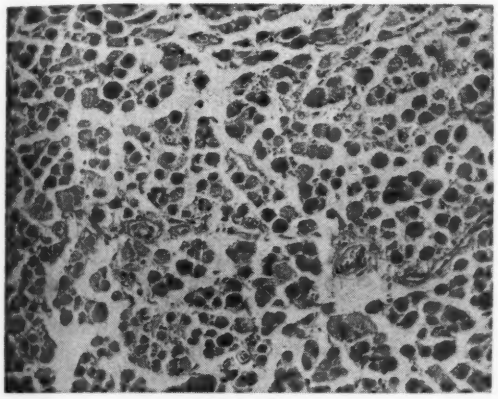

Figure 22

Extraocular muscle from a patient with biopsy proven temporal arteritis showing marked atrophy of the muscle. This patient also had bilateral central retinal artery occlusions, and thrombosis of the terminal aorta, vertebral and coronary arteries, giant cell arteritis elsewhere but not in this section x 110 (AFIP Acc. No. 747505).

Tumors Involving the Extraocular Muscles

Any study concerning the extraocular muscles and systemic diseases must include at least mention of tumors. The ocular muscles are very frequently involved as a result of paralysis of nerves, and from pressure of intraorbital tumors either primary or from tumors which have extended to the orbit from the cranium. A small minority of tumors involving the muscles originate from muscle tissue. Reese states in his textbook only twenty-five cases of "clear-cut" rhabdomyosarcomas have been reported (see Fig. 23). There are, according to Reese, three related lesions: (1) lesions containing adult striated muscle fibres arranged in an orderly manner; these are properly termed rhabdomyomas and are benign tumors, (2) lesions containing adult muscle tissue also evidences of inflammation; such tumors are granulomas, (pseudotumor), (3) tumors containing adult muscle tissue and in addition fibrous and nerve tissues; these probably are mixed tumors. A great majority of the sarcomas which originate within the orbit arise from other mesodermal structures — connective tissue, periosteum or fat.

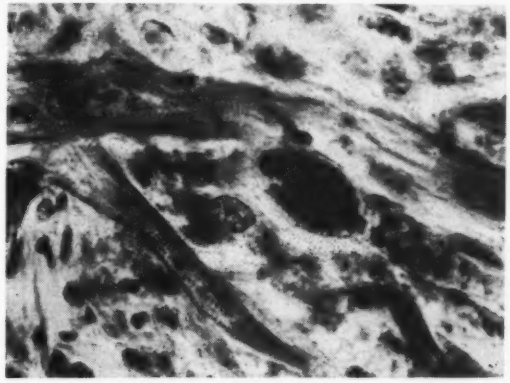

Figure 23

Rhabdomyosarcoma. Ocular Muscle. Stained with phosphotungstic acid-hematoxylin x 600. Note formation of muscle striations (from Wilmer Institute Pathology Laboratory)

In the Johns Hopkins Hospital electromyography is being done on such cases as have been described in this paper. It seems possible that ultimately such a method of examination will hold real value in diagnosis. At this time it has not added materially to our diagnostic capacity. We hope it may do so in the future.

This paper does not lend itself to summarization, but several generalizations can be made: (1) Dissimilar diseases may produce remarkably similar changes in muscle. For example, note the appearance of focal collections of lymphocytes in myasthenia gravis and in myotonic dystrophy. (2) The frequent lack of specific diagnostic features in muscle biopsies, plus the fact that muscles may not be uniformly involved by the disease process (and therefore a small sample may not be representative of the whole muscle) render histologic interpretation a difficult and specialized problem. (3) The principal involvement in muscle disease is either at the nerve nucleus, in the nerve, at the myoneural junction or within the muscle itself. Such a clinical grouping may have value.

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Medicine

Long-Term Anticoagulation in Coronary Artery Disease

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Soon after the isolation in 1939 and synthesis in 1940 of Dicumarol by Link and co-workers there arose an intense interest in the anticoagulant properties of this drug, and from 1941 on there have appeared studies on animals and men to demonstrate its prophylactic value in thrombo-embolism. From the outstanding study of Wright and others for the American Heart Association in 1946 there came the demonstration that in acute myocardial infarction treatment with anticoagulants reduced mortality by 50% along with a sharp reduction in further thrombo-embolic episodes. Although there have been criticisms from many a vantage point, which criticisms have been on the one hand idiosyncratic and temperamental and on the other reasoned and thoughtful, it is fair to say that this treatment is accepted almost routinely by a majority of physicians. But the very nature of the rationale of treatment in acute thrombosis of the coronary arteries provoked further adventure into long-term anticoagulation, for surely the principal purpose of short-term anticoagulation was to prevent extension and propagation of the clot and to prevent allied thrombo-embolism. If this were the case, then it followed that, perhaps, such treatment might be extended for months, years, or even the life of the individual concerned and so the concept of long-term anticoagulation was realized.

From the beginning it might be proper to define the purpose of permanent anticoagulation in coronary artery disease and this is, in a few words, to prevent further thromboses and embolism by permanent reduction of the coagulability of the blood to optimal levels. Although theoretically sound, the inherent dangers of anticoagulant drugs make it obligatory to assure that benefits from the use of these agents outweigh dangers therefrom to a considerable extent. It is apparent that on the whole the medical profession has accepted that such is the case. However it is likewise apparent that there has been perhaps a too uncritical approach to this question in that too few of the studies in the literature have presented adequate controls.

Let us, for a moment, return to the purpose of long-term anticoagulation and the consideration of whether or not it is a rational one. The success of prophylactic treatment in the acute phase has already been touched upon and serves as one motivating factor in the pursuit of long-term anticoagulation. A second compelling argument for the long-term use of anticoagulants centers about the factors of thrombosis and the process of atherosclerosis in the coronary arteries. It is first necessary to consider the incidence of thrombosis as the cause of a coronary occlusion, and here we arrive at a point in which there is an astounding divergence of opinion in the medical literature over the years. There have been a great number of carefully executed studies from 1923 to the present day and, in different investigations, the incidence of coronary thrombosis as a cause of coronary occlusion has varied from approximately 10% to 95%

*From the Department of Medicine, Deer Lodge (Veterans) Hospital, Winnipeg, Man. Presented at a Clinical Luncheon, Deer Lodge Hospital, May, 1958.

with an average of slightly less than 50%. It should follow, then, that if thrombosis of the elements of the blood is a factor in coronary occlusion in only 50% of cases, then anticoagulant drugs might be beneficial only in this same 50% of cases. However, the problem is more complex for there is a prevailing concept fostered principally by Duguid that there are two different types of atherosclerosis in the coronary arteries. First, cholesterol engendered and second, thrombogenic. This investigator believes that fibrous thickening of the intima of the coronary arteries can be the result of a gradual organization of an occlusive thrombus in the coronary arteries. This thrombus, by organization, shrinkage, recanalization and finally endothelialization, renders a histologic picture precisely like that of atherosclerosis. If such be the case, then the arguments for long-term anticoagulation are definitely strengthened. Duguid's opinions have been supported energetically by a number of observers both from a theoretical and experimental point of view, and many distinguished pathologists, by giving their support to this theory, have indirectly promoted the case for permanent anticoagulation. Finally, it may be stated that in experiments on the rabbit's ear-veins, Wright and others have shown that with the use of Tromexan, recanalization of a thrombus occurred on the average after about three weeks, whereas in control animals it was nearly three times as long before recanalization could be demonstrated. Here is further support for our concept. However, the consideration of theory must be swept aside before the more convincing criteria of clinical efficacy and, as will later be pointed out, such can only be finally accomplished with carefully controlled clinical study.

I would next like to consider briefly the practicality of permanent anticoagulant treatment, and this problem may perhaps best be approached by first considering the generally accepted contraindications to this type of therapy. These are briefly:

lack of patient co-operation;
absence of reliable laboratory facilities;
evidence of intracranial bleeding or increased intracranial pressure;
blood pressure consistently above 200/120 with Gr. 3-4 fundal changes;
recent extensive surgery;
advanced hepatic and renal disease;
blood dyscrasias with bleeding tendency;
active G.I. ulceration or active bleeding from other sites.

Having listed some of the more important contraindications, it is necessary to state that, on the whole, the treatment should not be considered extremely difficult or impractical, nor should there be rigidity in exclusion of patients for reasons of, let us say, inactive peptic ulcer or mildly impaired hepatic function and, although hemorrhagic phenomena have been made much of, if one excludes very minor incidents such as mild nose bleed, bleeding gums and bruises, the incidence of significant hemorrhage is probably less than 5% and is rarely dangerous. This is not to gainsay the fact, however, than an occasional death may be caused by the treatment itself. With a modicum of experience and with proper indications, facilities and co-operation, the ease of institution of a satisfactory program can not be doubted and does not constitute any obstacle to a planned study. It has been repeatedly demonstrated that permanent anticoagulation is eminently a practical possibility.

Before a consideration of the present study at Deer Lodge Hospital it may be valuable to briefly reconsider some previous studies of long-term anticoagulant therapy. Probably Nichol, in 1944, began the first serious cardiological investigation and from then several Scandinavian investigators, including Owren, Waaler and others, have conducted studies. To me the most interesting facets of these studies have been that they were almost universally inadequately controlled (or if they have been controlled the latter have been constituted by retrospective analyses) and that the studies have almost universally shown favorable results.

Of the uncontrolled studies one of the most interesting is that in which ten American cardiologists, headed by Nichol, combined the results of their treatment to include 1100 cases of single and multiple infarctions and of impending infarctions. The authors concluded that long-term anticoagulant therapy reduces the mortality in patients with a single infarct or multiple myocardial infarctions to a significant degree. Of the controlled investigations perhaps the three most interesting are those by Suzman and colleagues from Johannesburg, the investigations of Manchester in the United States and Bjerkelund's study from Norway. The first-mentioned study consisted of 208 patients with infarctions who, having had anticoagulants in the acute phase and having survived the first three months, were continued on treatment for periods up to 76 months. The controls were 88 patients who were treated only in the acute phase of the infarction and were observed for similar periods. Although there was a considerably lower mortality rate with fewer recurrences of infarction in the treated group, this study is open to much criticism on the following bases:

1. That there was not pre-arranged selection of control and treated groups;
2. That a considerable number of the treated group, for unstated reasons, concluded their treatment;
3. That control patients were not followed so closely in the clinic as were treated patients.

These criticisms are mentioned in some detail because they are of importance in almost every study that has been undertaken thus far.

The second mentioned study, that of Manchester, in which more than 550 patients were followed for

almost ten years, was more satisfactory in that control was more rigid. Here too there was a decidedly favorable effect in the treated patients.

Perhaps the most carefully planned and most significant of all the investigations thus far is that of Bjerkelund in which there were 237 cases, of which 119 were treated and 118 were controls. Careful planning in this study assured that patients were allotted by chance to the two groups and that ancillary care was almost identical. This study is of considerable interest not only in that it was carefully carried out but that the intensity of the anticoagulant treatment was carefully documented and it was shown that approximately 90% of patients were almost constantly adequately anticoagulated. Accordingly, the treatment must be considered to have been both intensive and satisfactory. Indeed, it is to be questioned that in the present state of our knowledge a more satisfactory anti-thrombic effect can be attained without greatly increasing the hazard of treatment. It is to be understood that in the control group in this study, anticoagulants were given only as short term treatment of recurrent infarctions. The authors concluded that the force of recurrence of infarctions for patients under the age of 60 was significantly higher in the control than in the treated group the first year of the study. Over the age of 60 the difference was not statistically significant, and after twelve months there was no definite difference, either over or under 60.

Again the mortality rate in patients under 60 years of age was significantly higher in the control group than in the treated group in the first year of treatment. After 60 there was no significant difference, nor after twelve months was there a difference.

The authors found no convincing differences against attacks of angina pectoris in either the treated or control groups. Their conclusions were strikingly different than those of any other comparable investigation and in view of the thoroughness of the study, they are considered to be so important that they are quoted verbatim:

"Although the view usually held previously has been that treatment is especially indicated in patients with recurrent infarction, in the worse cases after severe infarction with a tendency to heart failure and thromboembolic episodes, this investigation has shown that it is primarily the younger patients and those who have only had one infarction who benefit from this form of treatment. This is reasonable when it is remembered that the treatment is primarily prophylactic — not curative. Paradoxically it can therefore be said that while short-term treatment of acute myocardial infarction is primarily indicated in the so-called 'poor-risk' cases, long-term therapy is primarily indicated in the 'good-risk' cases."

I think, by now, it is fair to state that the generally accepted view in the reported literature is that there is indeed a place for long-term anticoagulant treatment and that most authors have been enthusiastic. There is, however, a real problem in the matter of selection of cases for this treatment. I would like now to briefly consider our own group at Deer Lodge Hospital, but not in very great detail for the reason that our study also has, unfortunately, been uncontrolled and is, to date, a quite minor one, since it comprises only a small number of cases. Although I do not propose to carefully review all aspects of these cases, I would like to mention certain features which seem of interest.

The study conducted at Deer Lodge Hospital in the past year or so has comprised 45 cases. Of these, three suffered from peripheral vascular disease, three had rheumatic heart disease with multiple embolization. There was one case of idiopathic thrombophlebitis with pulmonary emboli in a young man, one case of basilar artery insufficiency and one case of internal carotid thrombosis, a total of nine cases, leaving 36 cases with coronary disease for analysis. Of these 36 cases, two were excluded because of very irregular attendance at clinic. There remained 34 cases of coronary artery disease to be analyzed. Of these cases, 33 were male and one female. Their average age was 55.6 years with a range of 36 to 78. Of the 34 cases, twelve had had multiple (two or more) myocardial infarcts, five had one infarct and one other non-coronary thrombo-embolic episode. Ten patients had had one infarct and severe angina pectoris, five patients had had one infarct alone, and two cases had severe angina pectoris alone. The average patient day treatment period to the time of analysis was 162 days, a period considered to be too short for firm conclusions.

In this period the following observations were made. First, good control was generally easily obtainable. The object was to obtain a Prothrombin Time of between 20% and 30% (Quick one-stage method). Patients were requested to visit at intervals of from two to three weeks. In the six months' treatment period in this group of patients there were nine or ten inconsequential bleeding episodes, there was one major hemarthrosis for which anticoagulants were only temporarily discontinued and then resumed with no further difficulty. There was one 74 year old man whose anticoagulants were permanently discontinued because of rectal bleeding and anaemia. One patient died while on anticoagulants, presumably of staphylococcal septicemia and pulmonary edema. There was no overt hemorrhage in this case, but latent hemorrhage might have been present. There was no necropsy. It is fair to state that to date hemorrhage has been a relatively minor consideration.

There have been four deaths in this period. The first patient died at home. There was no necropsy and it is felt that no comment can be made. The second patient has been briefly delineated above.

The third patient was a very obese 50 year old man with intractable angina pectoris and long-standing pyelonephritis and hypertension. Necropsy revealed death to be due to acute heart failure. The coronary arteries were severely atherosclerotic. There was an old recanalized thrombus of the left and right coronary arteries. The fourth death was in a young man with a history of avitaminosis, nephritis, hypertension, heart failure and hypercholestrolemia, who died of an acute posterior myocardial infarction, while apparently adequately anticoagulated. His Prothrombin Time the day before death was known to be 30% of normal. Necropsy revealed, among other things, severe atheroma of the coronary arteries with old and recent thrombi of both coronary arteries. I will only say in comment here that even the most enthusiastic advocates of anticoagulants have not denied that thrombosis may occur in severely atheromatous coronary arteries even with optimal anticoagulation as we understand it now. There has only been one other recurrent infarction in a member of this series and this occurred during a visit to California when Danilone was not being taken regularly and it is documented that the Prothrombin Time the day before his infarction was 85% of normal.

Having briefly described the current status of the group at Deer Lodge Hospital, and having carefully eschewed major conclusions which I feel are definitely not justified (other than the practicality and safety of such a program) I would like to conclude by offering for your consideration some personal opinions about the agents under consideration. These opinions, I would emphasize, are not capable at the present time of complete substantiation.

1. Anticoagulants have no effect on the pain of angina pectoris, whether mild or severe. The real pain of angina becomes, in some sensitive individuals, so inextricably intertwined with the precordial heaviness or devilish prick of anxiety that the pain pattern tends largely to become difficult or impossible of analyses. A confident word from a competent physician, along with a pocketful of pills, cannot fail to have an effect. I have personally never suggested to a patient that anticoagulants would relieve his angina and I have never heard one of them say that they had. For a short while the odd one has claimed relief, but the distress has always returned. In the meantime in the patients in this series there has been no definable change in angina pectoris. This I would emphasize is not to say that anticoagulants have no effect on the long-term prognosis of angina pectoris. The matter is not yet settled.

2. The second opinion which I would place before you is that the indications for starting a patient on long-term anticoagulation, it being understood that ancillary conditions are ideal, are as follows:

A. A second myocardial infarction.
B. Any thrombo-embolic incident in an individual who has previously suffered a myocardial infarction.
C. The case of an individual who has suffered only one infarct but who has a severe infarct with a complicated course, a bad family history, or who has suffered the onset of unremitting angina pectoris or so-called impending infarction after recovery from the initial infarct.
D. In coronary artery disease in the name of ethical investigation with the patient fully cognizant of the pros and cons, not having received a slanted point of view.

3. My third opinion is that permanent anticoagulation is, so to speak, here to stay in one form or another until the twin scourges of atheroma and thrombosis are otherwise eliminated. The purposes of further controlled studies seems to be to clarify the indications for this measure and to establish its optimal degree. To cite an example, perhaps the best controlled study to date (Bjerkelund) is the most disturbing. I have already told you that he considers the younger individual with his first infarct the best subject for this treatment. On the other hand, only recently Katz, in an excellent study of almost 300 cases of myocardial infarction has given cheer. After two months' survival of an infarct (immediate mortality 23%) 66⅔% were alive at the end of five years, 40% at the end of ten years, and 10% at the end of fifteen years. The matter, of course, requires clarification.

Finally, a word regarding dissenters. They are caught up in a veritable flood tide and stand in danger of drowning. The principal opposition to anticoagulation in general has come from a small number of individuals whose main arguments reside in unsubstantiated ex cathedra statements. Indeed, the literature is remarkable for the paucity of protestations. On the other hand, it would be unfortunate for the medical profession to clutch permanent anticoagulation without repeated and adequately controlled studies whose chief purpose should be clearly to define the indications for, limitations of, and hazards of this form of treatment.

Pathology

Use and Abuse of Laboratory Services

D. W. Penner, M.D.

The practice of medicine in the last twenty years has seen a marked increase in the use of and the dependency on laboratory services. As more laboratory services become available fewer and fewer laboratory procedures are being done by the patient's own doctor. Especially in the larger laboratories more complex procedures are being done with expensive and complicated equipment. The specialty of Pathology in Medicine is rapidly expanding and the number of laboratories in Canada have increased and expanded. The National Hospitalization Plan with its inclusion of diagnostic services, first within hospitals and later to be extended to the out patient area, will produce even greater demands for space, equipment, technicians and pathologists. With all these rapid changes it is probably correct to take a critical look at the use and abuse of laboratory services.

Availability of Service

Before a service can be used or abused it must be available. How available are laboratory services generally in Canada and especially in the Prairie Provinces? Great progress has been made, but there is still a very definite shortage of laboratories especially in rural areas and smaller urban centers and an even greater shortage of pathologists and trained medical technologists. It is relatively easy to build and equip a laboratory. It is far more difficult to train and keep professional staff. In Canada a problem other than training professional staff is to keep them in our country. In Manitoba a substantial number of the technicians trained migrate to the U.S.A. In order to get a stable technical service it is important to encourage men to enter the profession and to provide them with wages and working conditions which are competitive. In order to get doctors to enter this specialty it is important to make pathology comparable to other medical specialties, and this in the future will mean the operation of laboratories on a fee-for-service basis. It is the duty of the pathologists to see that standards are maintained and improved and that everything is done to increase facilities in all areas of the country where the need exists.

Use of Existing Services

Are the existing services used to the best advantage of the patient? This question cannot be answered by a single yes or no answer, and obviously it varies greatly from doctor to doctor and area to area. In the past, and even still for those patients not admitted to hospitals there is an important economic factor. This factor tends to work both ways — laboratory services tend not to be used when the patient pays for them and tend to be overused in any pre-paid insurance plan. Generalization can be very wrong but I would hazard the opinion that at the present time there is still an overall under-use of laboratory services. For the future our major problem in the pre-paid plans is not over-use but faulty use or abuse. The proper use, no matter how great, can never be an overuse or abuse, although, of course, too great a demand can overtax the facilities and result in lowered standards.

An important question today, and becoming increasingly important is the principle of the use of routine procedures or tests as opposed to the ordering of procedures as clinically indicated. Virtually all large institutions now have routine urinalysis, routine chest plates on admission, routine serology for syphilis, routine throat swabs in children, routine blood counts etc. Each one of the procedures was set up on the assumption that by so doing the standard of medical care would be raised. Most of these procedures were also instituted when it was not the practice in medicine to use laboratory procedures as frequently as now. Routine urinalysis could protect an undiagnosed diabetic from having major surgery, etc. There is a great danger in the use of routine procedures. Clinicians can fall into a false sense of security and maintenance of high laboratory standards in volume routine procedures becomes a real problem. A recent check on some aspects of routine urinalysis brought to light some disquieting facts. Many routine admission urinalyses were not being submitted until the second or third day of admission only too often after the operation for which the patient was admitted had been performed. Physicians were not seeing the reports, often until discharge on the short stay patients, and occasionally the reports were not available until after the discharge. Every routine laboratory procedure in hospital or in a doctor's office should be subject to careful periodic review and if it fails to achieve the desired aim, or is economically unjustified, the faults should be corrected or the procedure dropped. The clinicians must also have assurance that the laboratory standards are being maintained, in spite of a large volume of routine procedures. Ten years ago it was routine practice to have routine eye cultures on all patients coming to surgery in ophthalmology and routine throat cultures on all patients admitted to the pediatric wards. A review of the results of the preceding five years was undertaken, and it was found that not a single case of unsuspected diphtheria had been reported and that irrespective of the bacteriological report on the eye cultures, the operation planned was always performed.

Abuse of Laboratory Services

Laboratory services are of greatest value to the patient if they are used as a consultation service to assist in the clinical diagnosis and treatment of disease. They must never be considered a substitute for clinical diagnosis. In reviewing a number of charts of patients coming to autopsy it became painfully obvious that in too many instances hundreds of dollars worth of laboratory procedures were ordered which could serve no useful purpose for the patient nor could they be justified in the name of research or teaching. As the clinician gets farther and farther away from the actual participation in laboratory procedures, as the procedures themselves become more complex and once the economic factor has been eliminated at the patient level, this will become a greater and greater problem. There are a number of points to consider: knowing what procedures are available for the particular patient's problem, limitations of the laboratory procedure, proper interpretation of the results, proper application of the interpretation to the clinical case. For example, in an acute abdomen in which acute pancreatitis is suspected — what procedures are available which might lead to the diagnosis? Having decided that serum amylase determination might be of value, the accuracy or limitations must be known and the result interpreted in respect to the specific case. Not long ago we did an autopsy on a case of acute abdomen in which a high serum amylase was reported. In spite of the fact that the finding did not quite fit the clinical features of acute pancreatitis, it was presumed to be diagnostic and therefore, the patient was not explored. He died of mechanical small bowel obstruction. It is not always appreciated that very high serum amylase levels are not unusual in high small bowel obstructions and that moderately elevated levels occur in a great variety of conditions including pancreatitis.

Many laboratory procedures are non-specific, for example, the sedimentation rate. The majority of "tests for sugar" are in fact tests for reducing substances in urine and not specific for sugar. Certain procedures have a limited technical accuracy and, therefore, small variations have no meaning in following the clinical course of the disease. For example, prothrombin time increase or decrease of 5 or even 10% may well be due to the limitation of the procedure and not to therapy.

When it comes to interpreting results it becomes of greatest importance to know the normal or physiologic range for the procedure and to know the possible significance of the results reported. Very few laboratory procedures are absolutely diagnostic, and results must always be interpreted in relation to the specific patient. Recently an autopsy was performed on a small child who was admitted to a small country hospital with a history of having swallowed 100 aspirin tablets. The child on admission was considered to be a case of aspirin poisoning, but a routine urinalysis was reported as containing large amounts of sugar as well as showing ketosis. The patient was then treated for diabetic ketosis but subsequently died. Review of the case revealed that the test used for the presence of sugar gave an atypical reaction with the child's urine. This was wrongly interpreted as positive.

When discussing the proper use of laboratory services it is important to not only consider the clinician's use but also the role of the pathologist who provides these services.

Laboratory Standards

The pathologist and his laboratory are often very active in assisting to maintain standards of practice of medicine in a hospital. The clinician has every right to demand and expect that the pathologist will maintain an equally high standard of laboratory service. As a pathologist it is with reluctance that I have to admit that there is great room for improvement in this field. Only too often new apparatus is not adequately standardized, or having been standardized, not cleaned periodically. A recent survey of such a common procedure as hemoglobin determination in Winnipeg was revealing. It was noted that there often was a significant difference in the hemoglobin as reported by the W.G.H. and the hemoglobin performed outside just prior to admission.

Laboratory Induced Disease

Naturally an inaccurate hemoglobin can result in a false diagnosis of anemia and result in costly or even dangerous therapy such as blood transfusions. But quite apart from this obvious laboratory error due to failure to maintain standards (new hemoglobin pipettes even those supposedly standardized commercially vary considerably) many another problem is becoming of increasing importance. In a recent editorial in the American Journal of Clinical Pathology (Vol. 30, page 163, reference at back, August, 1958) this subject is reviewed, and it is pointed out that misleading laboratory reports may be caused by technical errors due to substandard technicians with inadequate supervision, failure to use adequate controls, by improperly labelled specimens (especially in blood banking), confusion of patients with similar names, "fasting patients" who have eaten, etc. The indiscriminate use of screening tests may be interpreted as valid for a definitive diagnosis. The chief purpose of a screening test is to select cases on which further testing is to be done. Therefore, its chief value is negative, and all positive screening procedures must be most cautiously interpreted. Many of the tests for sugar in the urine are screening tests for reducing substances and not specific tests for glucose.

Various drugs induce false positives and these must be known. Streptomycin, broad spectrum antibiotics and large doses of penicillin can all give

rise to a positive Benedict's reaction in urine, and penicillin may produce a false positive trichloracetic acid test for albumin. Biologic false positive reactions in serologic tests for syphilis may antecede the symptoms of lupus erythematosus by a number of years, and cells indistinguishable from L.E. cells occur in serum sickness, following the use of hydralazine, and in penicillin hypersensitivity. Although the cephalin flocculation test has been accepted as a screening test for liver disease it has now been shown that up to 14% of healthy workmen tested yielded 3 or 4 plus reactions with the widely used Difco reagent.

In tissue diagnosis inadequate biopsy material or lack of clinical details may lead to an incomplete or even a wrong diagnosis. It should be remembered that a biopsy or tissue submitted for diagnosis is in fact a consultation to another doctor who is a specialist in the field of Pathology. Interpretation based on morphology alone cannot always be accepted at face value. There are a number of conditions, for instance, which result in a histologic picture indistinguishable from squamous carcinoma but are actually pseudo epithelomatous hyperplasia and not cancer. These occur in the epithelium overlying myoblastomas, in chronic fungus infections, associated with malignant melanoma, etc. Knowledge of the age and sex of the patient is often of the greatest importance. It is still not generally recognized that malignant melanomas do not occur before the age of puberty, yet these lesions may show all the histologic features of a malignant melanoma. Not too many years ago when a pathologist saw the histologic picture of a chronic granulomatous reaction he was reasonably confident that it was due to tuberculosis. Now we know that it is impossible to make a specific histological diagnosis on the basis of such a reaction unless we can demonstrate the specific etiologic agent by special stains or histochemical methods. A few of the differential diagnoses in these granulomas are tuberculosis, syphilis, fungus infections, Boeck's sarcoid, Berylliosis, and lipid foreign body reactions. In a case such as this it requires an active consultation between pathologist and clinician.

Summary

Some features of the changing patterns in the use and abuse of laboratory services have been outlined. A number of factors which can give rise to wrong or incomplete diagnosis have been reviewed. All of this points to the need for sufficient laboratories which must be staffed by adequately trained technicians who must be supervised by pathologists. It is imperative that there be close correlation between pathologist and clinician, and the pathologist in order to be of maximum service must be willing to see patients and not hide away in his laboratory and hand out reports, the correctness of which must never be questioned. A very good rule is that if a report does not fit the clinical features of the case, the report may be wrong and this should immediately result in a consultation between pathologist and clinician.

UNIVERSITY OF MANITOBA

Department of Obstetrics and Paediatrics

POST GRADUATE INSTITUTE

on

"Problems of the Mother and Baby at Term"

Auditorium, Medical College, Emily at Bannatyne

Wednesday and Thursday, March 25th and 26th, 1959

Visiting Guest Speaker

Dr. Helen Wallace

Professor of Maternal and Child Health, University of Minnesota (formerly Director of Bureau for Handicapped Children, New York City)

The visit of Dr. Wallace is made possible by a Dominion-Provincial health grant

Wednesday, March 25th, 1959
Auditorium, Medical College

Morning Session
Chairman: Dr. Brian Best

9.00 **Registration,** Auditorium Foyer.
Registrar: M. Whitenect.
Welcoming Remarks: Professor Brian Best, Acting Chairman, Department of Obstetrics, University of Manitoba.
Opening Remarks: Professor Harry Medovy, Head, Department of Paediatrics, University of Manitoba.

9.45 **Present Day Views of Toxemia:** Causes, Management, Recent Research Contributions.
Dr. A. W. Andison, Associate Professor, Department of Obstetrics.

10.30 **The Management of Placenta Previa.**
Dr. R. L. Willows.

11.00 **Observations on Congenital Malformations:** Incidence and Prevention.
Professor Helen Wallace, Guest Speaker.

Luncheon Break

Afternoon Session
Chairman: Dr. Bruce Chown

2.00 **Diabetes and Pre-Diabetes.**
Dr. John Moorehouse.

2.45 **Discussion on Antenatal Care.**
Chairman: Dr. Brian Best.
Dr. W. Friesen, Dr. A. S. Majury, Dr. E. G. Brownell, Dr. Jean McFarlane, Professor G. Sisler, Dr. Jean Webb.

Thursday, March 26th, 1959
Auditorium, Medical College

Morning Session
Chairman: Dr. Harry Medovy

9.00 **Hemolytic Disease:** Management of the Mother and Infant.
Dr. Bruce Chown.

9.30 **Respiratory Distress Syndrome in Infancy.**
Dr. E. J. N. Briggs, Assistant Professor, Department of Paediatrics.

Coffee Intermission

10.30 **Panel Discussion on "Infections in the Perinatal Period."** Three 10-minute papers by:
Dr. J. C. Wilt
Dr. K. Finkel
Dr. A. C. McInnis

11.00 **"What Can We Do About Perinatal Deaths"**
Professor Helen Wallace, Guest Speaker.

Luncheon

Afternoon Session
Chairman: Dr. A. S. Majury

***2.00** **Abruptio Placentae:** Implications, Complications and Expectations.
Dr. J. R. Mitchell.

2.45 **Questions and Answer Panel.**
Chairman: Dr. Brian Best.
Dr. Harry Medovy, Dr. Otto Schmidt, Dr. E. J. N. Briggs, Dr. Bruce Chown, Dr. W. D. Bowman, Dr. R. L. Willows, Dr. J. R. Mitchell.

Note:

*A practical demonstration in newer Labor Room and Nursery techniques will be conducted at the Women's Pavilion of the Winnipeg General Hospital under the direction of Miss K. M. Clarke, Supervisor, Women's Pavilion, starting at 1.30 p.m., concluding 2.45 p.m. Thursday afternoon. Register for this group at time of registration. This session is intended specifically for Graduate Nurses in charge of Labor Rooms and Nurseries.

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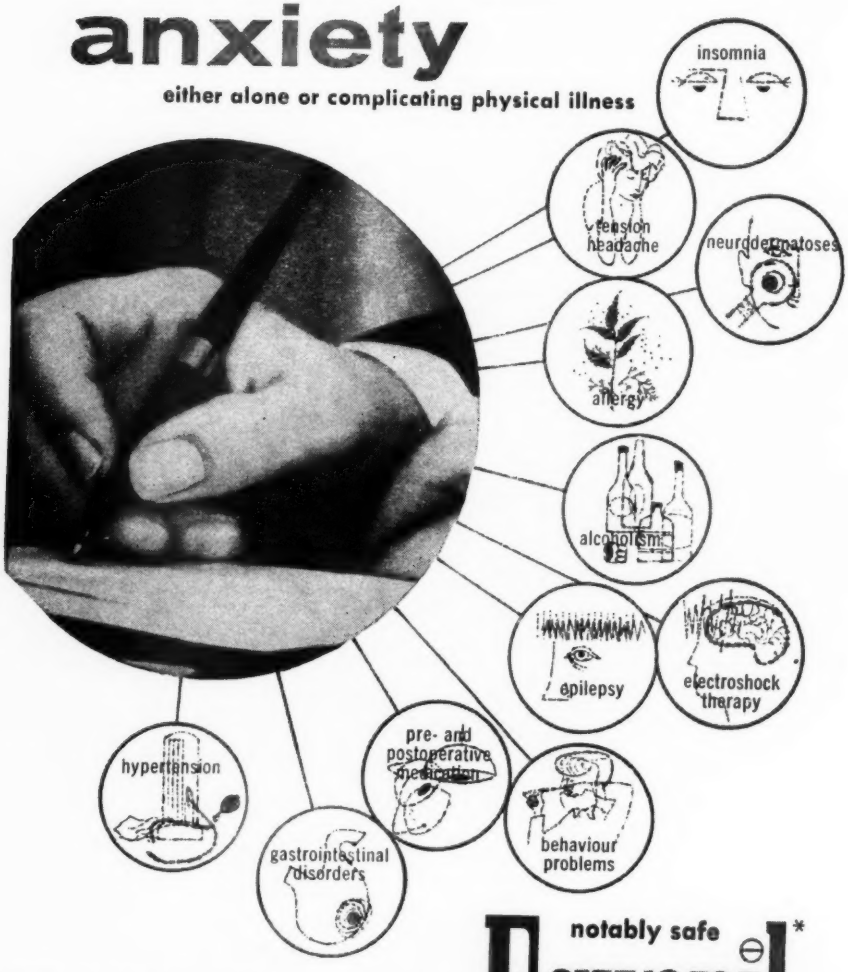

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Psychiatry

Preliminary Report On The Use Of Sodium Succinate in Schizophrenia

Peter Payne, M.B., Ch.B.
Brandon Hospital for Mental Diseases, Brandon, Manitoba

The discovery in 1943 of the psychic effects of LSD 25, Lysergic Acid Diethylamide[1], has reawakened interest in the effect of drugs on the personality. The claim has been made that Lysergic Acid and other hallucinogens produce a schizophrenic-like state in normal persons.

Many psychiatrists today believe that Schizophrenia is based on a primary organic pathology. It is, therefore, not surprising that research on hallucinogens has largely been directed toward a search for a possible biochemical aetiology of Schizophrenia.

Hoffer, Osmond, and Smythies[2], impressed by the similarity in the molecular structure of Mescaline and Adrenaline, investigated Adrenochrome, a metabolite of Adrenaline. They reported that Adrenochrome produced a temporary psychotic state similar to Schizophrenia. They, therefore, proposed that the symptoms of Schizophrenia are produced by the action of a substance similar to Mescaline, produced within the body during stress. They suggested that this substance could be a derivative of Adrenaline or a by-product of its production[3].

The suggestion has been advanced that Mescaline and other hallucinogens act through depressing oxidation in the central nervous system of Glucose, Lactate and Pyruvate.

The oxidation of Succinate, however, is not inhibited by these hallucinogens[4]. This would suggest that the symptoms produced by the hallucinogens could be abolished by Succinate, which would provide a substrate for oxidation in brain tissue when the oxidation of Glucose, Lactate and Pyruvate has been depressed by the Mescaline. Accordingly, Schueler[5] conducted a series of experiments on human subjects in whom he demonstrated a definite antidotal effect of Sodium Succinate on the symptoms of the Mescaline-induced psychosis. Smythies also confirmed that it exerts a blocking effect against LSD 25, Mescaline, etc.

If Schizophrenia is produced by the action of a substance similar to Mescaline, produced within the body during stress, and if such a substance acts through depressing oxidation in the central nervous system as Mescaline appears to do, then Succinate might reasonably be expected to antagonize it.

Therapeutically, Succinate has already been used in a small number of cases of Schizophrenia. Trautner et al used Succinate in oral doses of 4½ gms. daily. Of ten patients who had had Insulin Coma Therapy without deriving much benefit, six improved sufficiently on a combination of Succinate and E.S.T. to be able to leave hospital. The remaining four showed varying degrees of improvement, all being transferred to open wards.

Of eleven chronic cases treated, only one failed to show some improvement.

In a series of twenty-two successive admissions suffering from Schizophrenia, five recovered completely on oral Succinate alone. A further eight were apparently rendered completely well following the administration of E.C.T. in addition to Succinate. All showed some degree of good response. Only five were not improved sufficiently to leave hospital, although four of these were recovered to the extent of being allowed open ward privileges.

The Investigation

In view of the foregoing evidence that Succinate is a blocking agent in certain model psychoses and the hypothesis that the model psychoses and Schizophrenia have a similar aetiology, a pilot study was set up to observe the clinical effects of Succinate in Schizophrenia and, more particularly, on hallucinatory activity.

Seven male patients were selected. They varied in age from eighteen to fifty-two years. The length of hospitalization varied from four to twenty-four years. The clinical diagnoses were varied (see table), but in each case the patient was vividly and actively hallucinated.

Name	Age	Diagnosis	Length of Hospitalization
G.S.	18	S. Paranoid	4 years
J.E.	30	S. Mixed	10 years
L.M.	38	S. Paranoid	6 years
G.B.	38	S. Catatonic	18 years
J.P.	47	S. Paranoid	24 years
J.A.	49	S. Paranoid	10 years
R.D.	52	S. Paranoid	19 years

Psychiatric examination was carried out on each patient prior to and during the course. A daily chart was kept, by the senior nurse, on each patient, showing any changes in physical activity, hallucinations, delusions, accessibility, and mood. Recording commenced one month prior to the institution of treatment and was continued for twenty-eight days after the last dose. (Each patient also had C.B.C., Urinalysis, and Liver Function Tests performed weekly throughout).

The patients were treated for eighty-four days with 4½ gms. of Sodium Succinate. The Succinate was administered as ½ gm. tablets, each patient receiving 3 tabs. t.i.d., that is, 4½ gms. daily by mouth. As this study was in the nature of a preliminary investigation no controls were used.

During the first six weeks of the observation period no measures other than Sodium Succinate administration were used. During the second six weeks, four of the patients, namely, G.B., J.P., J.A., and R.D., received E.S.T. in addition to Succinate; this E.S.T. being administered twice weekly.

Results

Psychiatric

Patients receiving Succinate only, showed no improvement whatever.

After the institution of E.S.T. in addition to Succinate, one patient stated that whilst he still heard voices, they were less terrifying than previously. This patient has since responded to E.S.T. alone with a similar amelioration of hallucinatory activity.

Physical

No physical reactions, other than gastric irritation, were observed. Patient J.A. consistently complained of indigestion and nausea whilst on Therapy, which disappeared on cessation of treatment. There were no appreciable changes in C.B.C., Urinalysis, or Liver Function Tests.

Discussion

Experience with a limited number of patients treated with Succinate did not indicate that Schizophrenia, or more particularly the hallucinatory activity in Schizophrenia, is affected by the drug.

Forster et al[6], working with Frenquel, which is also reported to block LSD and Mescaline psychoses, similarly failed to confirm that Frenquel had any value therapeutically in the treatment of Schizophrenia.

This casts doubt upon an explanation of Schizophrenia similar to the biochemical explanation of the Model Psychosis.

Several authors have suggested that, included in the syndrome known as Schizophrenia, there may be at least two distinct conditions[7]: (a) One acute and with a symptomatology resembling that seen in the Mescaline psychosis and resulting from a Mescaline-like substance (possibly Adrenochrome) produced within the body. (b) The other more chronic due to some other cause or causes.

Osmond and Smythies[8] accordingly point out that the phenomena produced by the drug (Mescaline) should not be compared with those of the group of Schizophrenias en bloc, but that logically acute Mescaline symptomatology should be compared with that of acute Schizophrenia and chronic Mescaline symptomatology with that of chronic Schizophrenia. Since chronic Mescaline intoxication is virtually unknown, this comparison of chronic states cannot be made. Many psychiatrists have argued on the other hand that Schizophrenia is a single disease. Lucy's work on histamine tolerance in Schizophrenia would offer support for this belief.

If Schizophrenia is a single disease[9], then one would expect conclusions derived from investigation of chronic Schizophrenia to apply in some measure to Acute Schizophrenia. This being so, Succinate would be unlikely to be of value in the treatment of the latter, casting further doubt on the hypothesis that the Model Psychosis and Acute Schizophrenia have a similar biochemical aetiology.

It has been argued that the Mescaline psychosis is not a model of Schizophrenia, but approximates more closely to the toxic confusional psychoses.

Stockings[10] states that although many features of Mescaline Psychosis resemble Schizophrenia, the type and quality of the visual experiences relate it more closely to the toxic confusional psychoses.

Hoch[11] states that under Mescaline a complete Schizophrenic dissociation is much more prominent in Schizophrenics and latent Schizophrenics than in "normals." In the latter, the symptoms are more organic combined with some Schizophrenic.

Recent work by Trautner et al would lend support to this belief since they have shown that Succinate is of value in the treatment of toxic confusional states.

Conclusion

Whilst Succinate has been shown to be of value as an antagonist of certain model psychoses, the investigation herein carried out, whilst limited in its scope, did not indicate that Succinate was of any value in chronic Schizophrenia nor in the suppression of hallucinatory activity as a symptom in chronic Schizophrenia.

I wish to express my gratitude to Dr. Stuart Schultz, Medical Superintendent of the Hospital for Mental Diseases, Brandon, Manitoba, and to Mr. Art Russell, of the staff of the Hospital for Mental Diseases, Brandon, Manitoba, without whose assistance this investigation could not have been carried out.

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Psychological Aspects of Epilepsy

John Matas, M.D.

The importance of brain damage in epilepsy was noted by Hippocrates in 460 B.C. In the late 19th century Hughlings Jackson made a fundamental contribution to the clinical appraisal of seizures. He attributed them to excessive neuronal discharge and believed the pattern of seizure to be an indication of the site of the lesion in the brain. However, in spite of this it was possible for Pierre Clark in 1922 to put forth as an adequate explanation of epilepsy, a theory that the seizure was an expression of a wish to return to the womb, i.e., of being born again. Of course, the advent of the E.E.G. and work such as that of Wilder Penfield and his associates supported Hughlings Jackson's theory.

In reading and thinking about the psychopathological aspects of epilepsy, one is inevitably led to the consideration of temporal lobe epilepsy. In the last few years there has been much written on this subject, and many of the articles on epilepsy, in the psychiatric journals, are on this topic. The full impact of the expanding knowledge of lesions in this area of the brain has not yet been felt and integrated into psychiatric thinking. I am referring here to such facts as patients with lesions in the temporal lobe having as part or as the whole of their seizure, emotions such as fear, terror, sadness, loneliness. It is interesting to note that so far neither localized epileptic discharge nor electrical stimulation is capable of awakening anger, joy, pleasure, or sexual excitement. Lesions of the brain may also alter perception, resulting in erroneous judgments, in illusions, of size, distance, sound or sight, intensity, strangeness or familiarity. Hallucinations occur which resemble dreams in that they are not altered perceptions of present experience like illusions. The content of the hallucination is likely to be independent of the environment. It may be a vivid memory or a dream during which an awareness of the individual's environment may be retained. Different modalities of sensation may be involved in hallucinatory experience. The occurrence of coordinate movements like licking, sucking or more integrated ones have long been known to occur in relation to lesions of the temporal lobe.

It is not a big step to take from studying the type of case with illusions and/or hallucinations to the perplexing borderland between epilepsy and psychopathic behaviour. Recently, Ostow in New York, found electrical changes accompanying changes in affect in an obsessional patient. This leads Denis Williams to mention the disordered relationship with society observed in some people who have electrical disturbances in the temporal lobe. The neurologists, he feels, can consider the conceptual difficulty that these people have in much the same way as he considers parallel but less complex disturbances in the conception of the environment which subjects with parietal lobe lesions have. As bodily disorientation, e.g. astereognosis, loss of tactile localization, is a conceptual disturbance of the spatial environment, so is the distortion of feeling in the psychopath, a conceptual disturbance relating to his animate environment. Kubie has pointed out that it may be possible for neuroanatomic and neuropsychologic facts to be integrated with psychoanalytical theory. He feels that it is by studying patients with structural lesions who manifest psychological symptoms that we can begin to develop an anatomy of fantasy and dream life and overcome the organic functional dichotomy which now obscures this subject. Ostow has made an attempt to relate the findings of lesions in the temporal lobe with psychoanalytical theory.

It has been noted by various investigators that patients with seizures of the temporal lobe variety tended frequently to present in the interictal stage, symptoms of a psychiatric nature in the form of hysteria, psychoneurosis, obsessive-compulsive personality traits, or with psychotic episodes. No one has yet explained this phenomenon or the relation of these symptoms as they occur in temporal lobe epilepsy, to their usual occurrence, presumably in an effort to deal with intolerable anxiety.

In the rest of this talk I will consider the psychopathology of epilepsy under five headings.

The first of these subdivisions is the emotional problems that arise as a reaction to the seizure themselves. The experience of being overcome by uncontrollable force, some analysts say, may lead to submissive masochistic strivings. These strengthened by feelings of guilt for forbidden impulses may lead to a desire for being overwhelmed and punished with the aim of being forgiven and completely taken care of. This trend frequently acquires a religious coloring.

This is, of course, pure psychoanalysis, and other psychoanalysts go farther developing a thesis such as this. I have mentioned Pierce Clark earlier on. He states: "the paroxysmal experience renders the individual helpless and, on an organic basis by inhibiting and partly paralyzing higher centers, releases earlier infantile types of functions. Thus in a certain sense the individual goes through a replica of infantile development. This trend reaches its height in a notion of return to the womb and of being reborn." Bella Mittleman goes on to say: "It is to be noted that the fantasy of return to the womb goes in two opposite directions, as many of the dynamics of epilepsy may. One is an esape from the disappointments and frustrations and failures of mastery in relation to the adult world, the other is followed by the fantasy of re-birth with the idea of recovery from the destructive

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forces of illness, of becoming a totally new person, cured and effective."

Another idea put forth by the analysts is that the epileptic process may stimulate excretory and genital strivings. The relaxation of sphincters in the grand mal attacks, the automatic actions of self exposure and urination, they say, all point in this direction. What is patently visible in the paroxysms may be present in sub-paroxysmal intensity in other periods.

The second heading is the psychological reactions which arise in response to the illness in the sense that it is a continuing disturbance. This manifests itself in increased difficulty in carrying out certain activities and by an overreaction to certain environmental stimuli. The reaction to these primary disturbances may be increased aggression. The patient may be resentful over his internal difficulties, and become angry at himself. On the other hand, he may blame his environment, and become hostile and even paranoid. This is, of course, a common type of reaction seen in epileptics, and there is more than one suggestion that psychic causes are not the only ones at the basis of the hostility and irritability. Bridge points out that in children the irritability is often seen before the first seizure. From this he concludes that it is probably part of the epileptic process.

In addition to the increased aggression, the vague unlocalized disturbance may give rise to increased anxiety. The patient's uncontrolled reaction, vague discomfort and loss of efficiency lead to anxiety. This anxiety is further strengthened by fear and helplessness in the face of retaliation from the environment to which he is hostile.

Another reaction is inhibition and withdrawal. The patient wants to stop the function which leads to difficulties and wants to withdraw from the environmental stimuli which lead to distress and shut out the surroundings which he fears.

At least as pertinent as these observations is the difficulty the epileptic has in adjusting to the limitations put on him by his disease as it affects his acceptance by the community. This raises a host of problems regarding employment, marriage, children and contributes considerably to the hostility and anxiety. Many people feel that the epileptic personality is a reaction to these limitations, much in the same way as any person subjected to a similar degree of physical handicap from other sources might be.

The manifestations of the epileptic character are: irritability, combined with destructiveness in younger age periods. The patient grows self-centered, selfish and inconsiderate. He may grow especially susceptible to flattery and may boast childishly, with a shallow, at times sentimental and superficial interest in his environment. This interest is often religious.

The psychological explanation for the epileptic character is as follows: The egocentricity is a self absorption reaction to the vague discomforts and the anxieties as well as a compensatory attempt at self magnification in the face of feelings of deficiency. Once this trend is developed, its effects go in the same direction as the previously mentioned reactions to the primary organic disturbance of functions, namely, hostility toward the environment and withdrawal. Some analysts explain the dementia which occasionally occurs in epilepsy as the result of this withdrawal process. They say that this process may lead to impairment of memory for recent events because interest in associative thinking is reduced. The narrowing of the field of attention which occurs in epileptic dementia could fit into such thinking. Perhaps the slowness of thinking, the circumstantiality can also be explained on indifference and withdrawal. The perseveration is usually explained as being a manifestation of "organic orderliness," as described by Goldstein, who has pointed out that patients with organic cerebral change often try to order their life carefully in order to be able to deal with their environment more easily.

As evidence that the dementia is psychological, Clark reports a case of a fairly well advanced dementia improving with psychotherapy including environmental manipulation. This is, of course, a thesis that cannot be readily accepted, as it is a well known fact that fits do impair intellectual functions on an organic basis. This is something we see every day as a result of the electrically induced convulsions. We know that changes in intellectual functions are roughly proportional to the number and frequency of the fits. Further, the changes in the E.E.G. parallel the changes in intellectual functions. The more fits, the greater impairment of memory and the grosser the E.E.G. changes. We also know that the degree and duration of the disturbance increases very much, if treatments are administered in quick succession. The exact pathology is not known. There is experimental work indicating that vascular spasm occurs during a fit and it is also suggested that the greatly increased cerebral metabolism in a fit is followed by anoxia. Another possibility suggested is that epilepsy is a progressive disorder and deterioration occurs irrespective of the number of fits. Against this argument is the fact that personality and intellectual changes occur in those who have a large number of fits close together in time.

Clark's case is suggestive of the many instances of schizophrenia who had lead withdrawn, vegetative existences and improved when put on a "total push" regime.

Gibbs and Gibbs point out that the manifestations of the epileptic character are most likely to be seen in patients with psychomotor epilepsy.

The third heading under which I am considering psychopathology is the fact that strivings and conflicts may become interwoven with the epileptic

process and influence the pattern of seizures. It has been pointed out in the literature that the psychic experiences — what is heard, seen or otherwise experienced in seizures — are most frequently related to trivial occurrences of every day life situations. However, Sisler described nine cases of "running-fits," whose running seemed to be related to conflicts in the family. Seven cases are reported from Mayo's, by Rodin et al, in which the thoughts occurring in the psychomotor attacks were connected in one way or another with the patient's ordinary thinking, and in two cases with the patient's wishes. In one of these, the patient had a visual hallucination of a wrestling match. This patient was particularly interested in wrestling. In another of these, the patient had an auditory hallucination of music, and this patient's greatest desire has been to be a musician. Another patient had fantasies of Indians chasing him which seemed related to his living near a swamp supposedly populated by hostile Indians in his youth. A woman hostile to her child experienced a terrific pounding headache, and the pounding seemed to say to her: "Kill, kill, kill."

The fourth type of relationship between the illness and the total reaction of the individual is a commonly observed one. Emotional upsets are frequently seen to precipitate seizure and seizures frequently relieve emotional tension. One example that I had, which comes to mind, is that of a fifteen year old boy, who because of his limited intelligence could not obtain any other but manual work and was often out of work because of his physical immaturity. When he worked, seizure control was no problem, but when he did not, seizure control was impossible with any type of medication. The problem of mechanics of the emotionally precipitated seizure has not been solved. However, the close relationship, anatomically speaking, of the temporal lobe and the limbic lobe, which is supposed to have something to do with elaboration of emotions, is suggestive.

It is also a matter of common observation that when seizure control is at its best as a result of medication, for some other reason irritability is at its worst. It is a well known fact that if an epileptic under control starts having many seizures with the same medication, the first place to look for the basis of this is the difficulties in the environment.

It is instances like this that have given rise to considerable speculation around the hypothesis that epileptic convulsions are tension reducing mechanisms and represent an explosive discharge of the lower brain centers, resulting in the discharge of emotional tension.

I came across a report of one case in which there were no other means of precipitating seizures except by an emotional upheaval. In this case the most effective way was to suggest the conflict under hypnosis.

The basic concept is one that analysts have described for some time, and has been referred to above. Fenichel, in his book, describes the seizures as "affect attack." A means of discharging dammed up emotion through the C.N.S. rather than through the autonomic system in predisposed individuals.

Sir William Gowers, in his text book on Epilepsy, published in 1901, states in a chapter on etiology: "of all the immediate causes of epilepsy, the most potent are psychic — fright, excitement, anxiety. To these were ascribed one third of those in which a definite cause was given."

Rows and Bond, in a monograph published in 1926, entitled: "Epilepsy, a Functional Mental Illness," reviewed the literature of the day, and the evidence of their personal experience with post war epileptic patients in a mental hospital in England, indicated that epilepsy is a mental disease and manifestation of an emotional conflict. It is explained in their chapter on treatment, that patients must be led to understand the nature of their symptoms and to learn the reasons for the attacks. They do not indicate what measure of success they obtained by use of their method.

Bridge, in his book on "Convulsive Disorders in Children," page 185, says: "whether or not the entire disease may develop on the basis of personality factors without the existence of a familial tendency, a brain injury and/or physiological disturbances which affect the brain, is still an unsettled point. We have gained the impression that this is a distinct possibility."

The last topic is the meaning of the attacks to the patient. Some reference has already been made to this, however, Mittleman gives the following list of meanings that an epileptic attack might have.

1) Escape from an unbearable situation.

2) Engaging in forbidden sexual activity.

3) Representing a state of anxiety, e.g., a patient's automatic acts consisted of lying on the side in a fetal position preceded by an aura of epigastric stuttering and trembling. The aura turned out to be a replica of a severe anxiety attack he had just preceding the onset of his epilepsy during a period of serious conflict with his oppressive father.

4) Fantasy of an aggressive act, including murder. The patient would run away from his father in pre-convulsive state and would worry after the attack whether he had actually killed his father. The most dramatic examples of the murderous epileptic experience, of course, are those of epileptic furor in which the patient actually commits a murder with complete amnesia.

5) Suicide. A patient whose attack started after he saw his mother hang herself usually either as an automatic act or in the past convulsive state, hangs his head and sticks out his tongue.

6) Experiences of destruction and re-birth. A patient in a post epileptic confusional state had the

feeling that she must die, but this dying was to be the beginning of a new life. She prayed and heard religious songs. Everything fitted into the notion of the destruction of the world. This destruction was to take place in her. The next morning she felt like a new person and experienced a strong urge for activity.

Epstein and Ervin reported two cases with psychomotor epilepsy which they had studied intensively. Their study illustrates some of the relationships between epilepsy and the person suffering from it. They concluded that the behaviour exhibited in the seizure of their patients, is dependent on past learning experiences and personality. This behaviour occurring in a milieu of altered cerebral functions is characterized by patterns of organization encountered in dreams—psychosis and hypnagogic states. The content of the seizure state was similar to the dream study and at times identical. The seizure, like the dreams, were found to represent motivated behaviour and to have meaning in terms of wish fulfillment and riddance. Seizure content, similarly, was dependent upon current emotional problems. Both dream content and seizure psychodynamic patterns involved areas in which there were conflict. Each of the patients had an overt psychotic episode in which the behaviour encountered was similar to that in seizures, and the conflict expressed was also similar.

The authors consider the seizure a pattern of behaviour and examined it in terms of motivation and adaptive value. In periods of psychological stress, simultaneous appearance of a destructive impulse and a wish to control this impulse, creates mounting psychological tension not immediately soluble in reality. The adaptive value of the seizure lies in serving as vehicle of discharging such tension.

Summary

Some of the relationships between epilepsy and the epileptic have been outlined. These relationships are a two way reaction. They involve the patient's reactions to the illness and its various manifestations, on the one hand. On the other hand, there is the influence of patient's thoughts and feelings as they influence the symptoms of the illness.

Study of the variegated manifestations of psychomotor epilepsy leads to speculation regarding the possibility of explaining some cases of what are now called neuroses and character disorders on the basis of a temporal lobe lesion.

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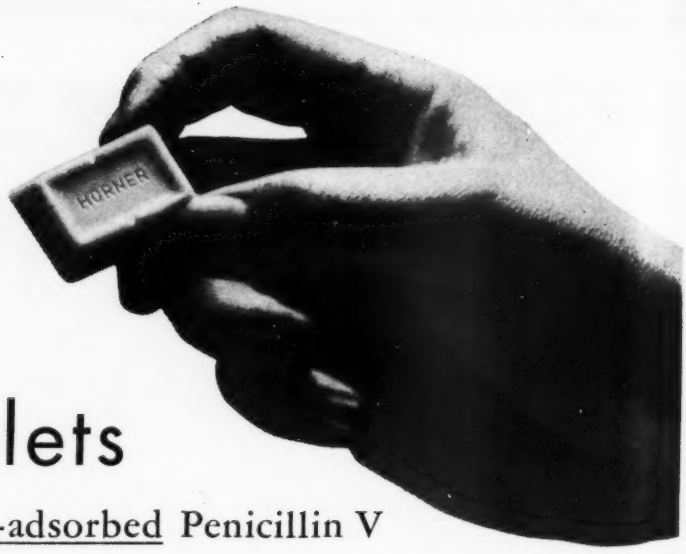

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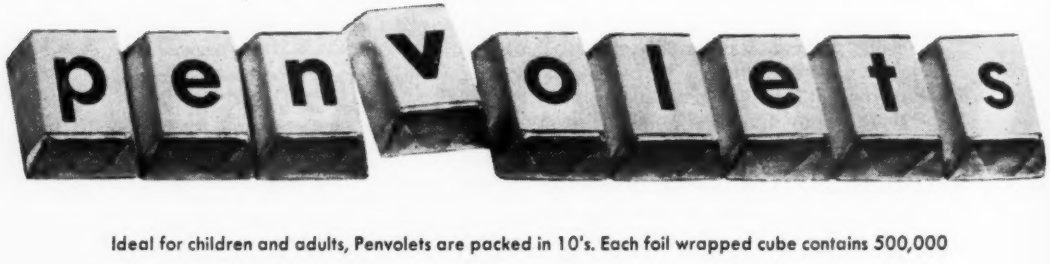

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Medical History

H. H. Chown

Third Dean of Manitoba Medical College

1859 - 1944

Ross Mitchell, M.D.

Few men have played a larger part in the building up of Western Canada than Henry Havelock Chown. For sixty-two years he lived in Winnipeg and saw it grow from a frontier boom town with mud streets and wooden sidewalks to the metropolitan city that we know today. He served as general practitioner, surgeon, medical statesman and medical referee and in each field he was a leader.

Like the Oslers, the Chown family originated in Devonshire and came to Canada as pioneers. Roger Chown and Sarah Thorn were born a few miles apart, married in 1820 and with three children sailed to Canada on the "General Wolfe" in 1832. They made their new home in the historic city of Kingston. This charming limestone city, strategically located, was the first capital of Canada (1841-1844) after the union of Canada East and Canada West. The founding of Queen's University in 1842 increased the importance of the city although six years later the population of Kingston was only 8,416 and of Canada West 725,879. Roger prospered. Other children were born into the family circle, and the parents strived to give each child a good start in life.

Edwin, the eldest, and his brother Arthur started a hardware store. Later Edwin and his partner Cunningham instituted the Eagle foundry to manufacture stoves and ploughs. For twenty years Edwin was an alderman of Kingston and for even longer, prominent in Sydenham Methodist Church. Meanwhile other descendants of Roger and Sarah were making their mark in business, Queen's University and the Methodist Church of Canada.

Henry Havelock Chown, a younger son of Edwin and named after the hero of the Indian Mutiny, was born February 16, 1859. He was educated in Kingston schools, Victoria College, then at Cobourg, where he received his B.A. degree and at Queen's medical school, graduating M.D. in 1880.

At that time the new province of Manitoba, "the gateway to the last West" loomed large in the public eye. Winnipeg had been joined by rail to St. Paul and therefore presented glittering possibilities and young Henry had the same pioneering spirit that had animated Roger and Sarah. For about two years he practised in the frontier town, then early in 1882 he left to acquire further knowledge and an English degree. A diary, written in pencil, details his activities between February 15th and July 13th, 1882. It is now in the Medical Library of the University of Manitoba as a gift from his son, Dr. Bruce Chown. Opening with his departure from Kingston via the Grand Trunk railway to Montreal and the Intercolonial to Halifax, he relates boarding the Allan liner "S.S. Peruvian." Smallpox was discovered on board, giving him an opportunity to assist the ship's doctor. The crossing took 11 days!

Arriving in London he secured lodgings, then hastened to the London Hospital, Whitechapel, where he was accepted as a clinical clerk. He had the privilege of working under such distinguished teachers as Dr. Andrew Clark, the Queen's physician, Frederick Treves, just beginning his brilliant career in surgery, Morrell Mackenzie, the laryngologist who attended Emperor Frederick of Germany, Hughlings Jackson the neurologist, Sutton, "my man!", Jonathan Hutchinson, Fenwick, Herman and others. On March 23rd at the Royal Institution he heard John Tyndall lecture on "Resemblances of Light and Sound;" on April 1st saw Oxford beat Cambridge on the Thames; on April 6th he met a fellow Canadian, Dr. Aikins of the distinguished Toronto family which was to give two lieutenant-governors to Manitoba.

On April 30th Henry Chown attended a crowded service at Westminster Abbey to hear Canon Farrar speak eloquently in praise of the life and work of Charles Darwin who had died eleven days earlier. On receiving a card from the Speaker he visited the House of Commons on the evening of May 23rd and heard a debate on "The Prevention of Crimes in Ireland" bill with Healy, Dillon, Parnell and O'Connor up. On May 28th he heard Cardinal Manning at St. Marys Moorfield.

"The London" was not the only hospital he visited. On June 9th he was at the Children's Hospital, Great Ormond Street; then went to the British Museum for an hour, next to King's College to see Lister. ". . . a fine gentlemanly well built man, full face, white side whiskers and hair turning grey . . . only a poor operator . . . removal of tongue for cancer." "Saw Watson Cheyne tie right vertebral artery for epilepsy." On June 28: "at the London, heard Dr. Whitla, brother of R. J. Whitla of Winnipeg." As became a well rounded man he went to the Adelphi on July 8th to see Booth in Richelieu. ". . . magnificent, finest I have seen." Two days later he and a friend "tramped over to Regent Street for exercise and hunted out tailor Dr. Osler had recognized." Shortly after that he and his friend invested in silk toppers. With his closely cut Vandyke beard, the topper and the Regent Street clothes he must have cut quite a dash! No doubt he was thus dressed when he appeared before the examiners for the L.R.C.P. On July 12th at the Samaritan Hospital he saw

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Thornton remove a fibroid tumor and a uterus containing 4½ months foetus. Among those present was Robert Emmett of New York. ". . . middle-aged gentleman, cool and quiet looking."

When he returned to Winnipeg the topic of discussion was the proposed Manitoba Medical College. Chown felt that the project was premature and he was not one of the incorporators of the School in 1883. By 1885 he was teaching anatomy there and thus began a connection which lasted till 1917. He became Professor of Clinical Surgery; then when Dr. J. W. Good went to the Yukon on "the trail of '98," he was elected Dean in 1900. In 1905 the University of Manitoba, which till then had been only an examining and degree-conferring body, erected the Science building on Broadway and established a Science Department with Professors Frank Allen (physics), Matthew Parker (chemistry), A. H. Reginald Buller (botany), Swale Vincent (physiology) and Gordon Bell (bacteriology). The Science Department taught students of the new premedical course, and the science of medicine, rather than the art, began to be stressed. Dean Chown was responsible for bringing to the Medical College in 1909 the first whole-time professor of anatomy, E. J. R. Evatt. In 1917 the College which, though affiliated was independent of the University, became an integral part as the Faculty of Medicine of the University of Manitoba. The property and equipment of the College, valued at $250,000, were turned over to the University free of debt. For years Dr. Chown had represented the College on the University Council; in 1917 he became a member of the first Board of Governors of the University and resigned as Dean.

His connection with the General Hospital lasted for 32 years. He was a daring and expert surgeon, always a little in advance of his time. He never wore rubber gloves but his hands were gentle, swift and skilful. He rose with the birds, liked to operate as early in the morning as possible and confided that he never approached a difficult or exacting operation without reading up the details immediately before coming to the hospital. To his credit stood the first ovariotomy and the first gastro-enterostomy (anterior) in Western Canada. To ensure the success of the former operation he purchased new linen for sheets and dressings and had the patient placed at his own expense in a private room. The gastro-enterostomy attracted so much attention that the Governor General of Canada who was then visiting Manitoba requested Dr. Chown, at a dinner in Government House, to draw a diagram of the operation.

After his marriage to Kate Farrell, a lady of charm and humour and devoted to her husband and sons, he lived in a frame house at the north-west corner of Donald and Ellice, and later at 263 Broadway near his beloved Manitoba Club. On the death of his wife in 1916 he was cared for by a Chinese manservant. His elder son, Charles, died in early manhood, the second, Dr. H. Bruce, is internationally known as a serologist. The late Dr. Gordon Chown was a nephew of Dean Chown and Gordon Chown, M.P. for Winnipeg South, is a grand nephew.

In his early years Dr. Chown read widely in Western Canadian medical history and on September 17th, 1915 he was persuaded to read before the Winnipeg Medical Society a paper on "Medical Men and Medicine in Western Canada."

When the Great-West Life Assurance Company was formed in Winnipeg he became a charter member. On his retirement from active medical practice he and his friend, Dr. R. J. Blanchard were the first medical referees of the company.

Other associations of Dr. Chown were with the 90th Battalion to which he was Medical Officer, the Children's Home and the Children's Hospital. In 1901 he was President of the Canadian Medical Association and at the annual meeting in Winnipeg he operated before his colleagues for the removal of a hydatid cyst of the liver, rarely found in eastern Canada.

In 1903 his Alma Mater, Queen's University, conferred on him the LL.D. degree, an honor which he prized highly. On the 60th anniversary of the University of Manitoba his name was proposed for the same degree but he modestly declined stating that one such honor was sufficient.

His later years were spent largely in travel, usually by air. In a humidor presented to him from the Ontario delegation in 1911 is his passport with visas stamped from Japan, China, Brazil, Argentine, Chile, Palestine, Egypt, France, Monaco, Colombia, Ecuador, Peru and Mexico. With Ulysses he could say: "Much have I seen and known." He liked to be up to the minute and to maintain his lively interest in men and affairs. He died on October 12th, 1944.

In all ranks of life he had many warm friends for he "did good by stealth and blushed to find it fame." He was the prototype of Dr. Towne in "The Viking Heart" by Laura G. Salverson and her "Confessions of an Immigrant's Daughter" was dedicated to him for his devotion to the poor. Henry Chown was indeed one of the makers of the Canadian West and more than any other he laid the foundations of the present structure of Manitoba's school of medicine.

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Editorial

S. Vaisrub, M.D., M.R.C.P. (Lond.), F.R.C.P. (C.), F.A.C.P., Editor

Pleasure

Even a cursory glance at the current medical literature will spot numerous papers and not a few editorials — the Manitoba Medical Review not excepted — on the subject of Pain. Yet the most thorough search will fail to find a reference to Pleasure. This, of course, is not surprising. Pain is a composite of sensation and emotion with an anatomical - physiological - biochemical apparatus that readily lends itself to scientific investigation. Pleasure, on the other hand, is a complex emotion, ill-defined and poorly understood, without a measurable organic component. Furthermore, while Pain leads her wretched victims to the door of the physician to whom they become a challenge and a constant preoccupation, Pleasure lets her happy subjects romp wherever they may, joyfully nibbling at the proverbial apples that keep the doctor away.

Why, then, should a physician concern himself with pleasure? Why indeed? Unless, of course, to discover that far from being a stranger to pleasure, he has been involved with it all along — to find that while engaged in a hot war against pain he has been fighting a cold war against pleasure, a war for which no obvious explanation is available. Perhaps the causa belli lies in the persistence of the puritanical association of pleasure with sin, or in a thinly disguised sadistic impulse. Whatever the cause, the propaganda war on pleasure is being fought on many fronts. Food, drink, tobacco, sex, work, leisure — all are under heavy attack. Let us take a closer look.

The pleasure most frequently and persistently under attack is the pleasure of eating. Between the modest restraints of a "balanced" diet for the pleasantly plump and the cruel restrictions of the practically foodless diet for the obnoxiously obese, there lies a wide range of rigid dietary regimes aimed against the pleasures of the palate. "Bland" diet for the gastric, "smooth" for the spastic, "rough" for the costive are but a few examples of the mild types of restraint. More restrictive are the "low" diets — low protein for the uremic and the failing hepatic, low fat for the atherosclerotic, low carbohydrate for the diabetic, low purine for the gouty arthritic. Absolutely enslaving are the "free" diets, of which the salt free diet for the hypersensitive and the failing cardiac is the outstanding example.

The attack on the joys of gustation is no longer confined to the sick and the gluttonous. It is spreading and now threatens the "average" eater. Propaganda campaigns against fat, ostensibly the chief culprit in atherosclerotic heart disease, menace the public with ominous dietary changes. The time is fast approaching when a Salisbury steak will be classed as "bootleg" and a buttered pancake as "contraband."

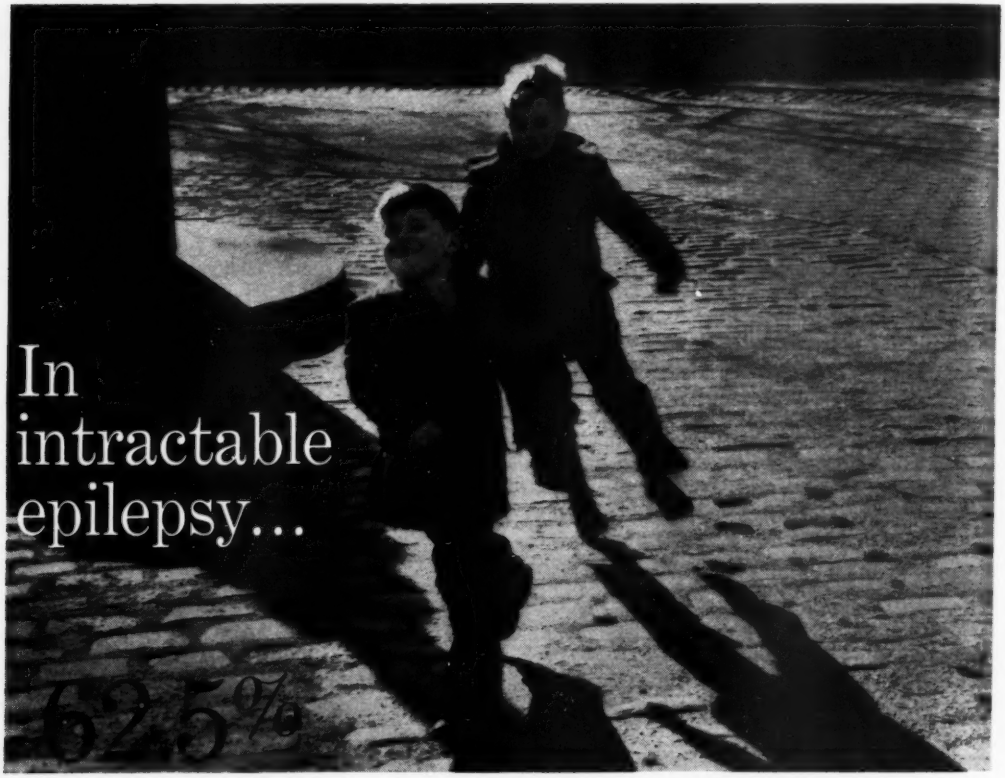
Next in line of attack are the pleasures of alcohol. Here, however, the thunder has been stolen by the laity. Alcoholics anonymous, temperance leagues, social agencies of various kinds have relegated the doctor to a relatively minor role as a joy killer. A similar situation obtains with regard to sex. Religious and social forces have taken the wind out of the medical sails, and are in charge of pleasure deprivation.

Much more vigorous is the medical assault against the joys of smoking. Previously confined to sufferers from smoker's cough, peptic ulcer, coronary disease and peripheral vascular afflictions, it is now threatening to involve everyone by dint of the recently discovered carcinogenic potentialities of the "filthy weed." The status of the physicians as the depriver par excellence in this area of enjoyment is unassailable.

When at a loss for pleasures of the flesh to attack, the frustrated physician can always turn against the joys of the spirit. The blissful state of ignorance offers a ready and vulnerable target. How simple it is to demolish the good spirits of the cheery patient coming in for a routine "check-up" by a remark about his blood pressure or his low blood count! How easy it is to tell the patient afflicted with a serious or even fatal malady, but blissfully unaware of its implications without "mincing words" or "beating about the bush" the bitter truth. How tempting to disregard the wisdom of Thomas Gray's admonition: "Where ignorance is bliss, 'Tis folly to be wise."

The forces unleashed by the doctor against the pleasures of the flesh and the spirit are not, however, always on the ascendant. Occasionally they lose ground. Bed rest, for instance, a measure intended to suppress the pleasure of ambulation is no longer popular. For centuries regarded as a sine qua non in the treatment of disease, it is now on the decline. In fact, the pendulum is swinging in the opposite direction, and now rest, leisure and inactivity are the principal targets for medical joy killers.

This most recent assault on the pleasure of loafing is based on experimental and statistical evidence which suggests that inactivity predisposes to degeneration of the myocardium and possibly to coronary atherosclerosis. Morris (Lancet, 2: 1053, 1953) and several other observers have produced statistical data to the effect that coronary heart disease is more prevalent and more deadly among



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the "light" than "heavy" workers. Raab and his associates (Advances Cardiol., 1: 65, 1956) have brought forth some evidence to support the thesis that the mechanism of the cardiac damage in the inactive is an imbalance in the neuro-humoral regulation whereby the cholinergic-vagal influences, which normally offset the harmful effects of the sympathetic-adrenergic activity on the myocardial oxygen consumption and mechanical efficiency, fail to do so during inactivity. Kraus (J. Am. Geriatrics Soc., 4: 463, 1956) named this condition "hypokinetic disease," Raab (Int. Med., 101: 194, 1956) nicknamed it the "loafer's heart."

It may be safely predicted that as a result of the concept of a diseased "loafer's heart" there will commence an intensive campaign against the joys of loafing. The last citadel of enjoyment will fall. Those who cherish the precious freedom of leisure and the delights of loafing will ponder wistfully whether, it may not have been better to "have loafed and lost than never to have loafed at all."

Ed.

Abstracts from the Literature

Administration of Glucuronic Acid to Icteric Newborn Infants: Gloria Jeliu, Rudy Schmid, Sidney Gellis. Pediatrics, January, 1959, page 92.

This article is a critical dissertation on the use of Glucuronic acid as a possible alternative to exchange transfusions for the treatment of neonatal jaundice. Contrary to the results of the New York group, it would appear that Glucuronic acid cannot be utilized directly for glucuronide function.

It is now accepted that indirect reacting bilirubin must be connected to its direct acting glucuronide for excretion in the bile. Bilirubin glucoronide is produced from glucuronic acid directly but from an activated form uridine diphosphate glucuronic acid. From uridine diphosphate glucuronic acid the glucuronic acid is transferred to bilirubin by an enzyme system which is present in liver microsomes (glucuronyl transferase). The administration of labelled glucuronic acid to humans failed to result in the excretion of isotopically labelled glucuronides.

There is now some evidence that the administration of glucuronic acid causes a redistribution of bilirubin from the vascular department into the tissues, producting kernicterus.

Monte Kowall.

◆

The Effect of Penicillin on Acute Rheumatic Fever and Valvular Heart Disease: Edward A. Mortimer, Jr., Charles H. Rammelkamp, Jr., et al. New England Journal of Medicine, 260: 101, 1959.

This article is a preliminary report on the effect of penicillin on acute and recurrent rheumatic fever. This investigation was sponsored by the Commission on Streptococcal Diseases and included all patients admitted to the Jose Joaquim Aquirre and Roberto Del Rio Hospitals in San Diego, Chile, from June to September, 1956. The diagnostic standards for admission to the study were almost identical to those employed in the British American co-operative study on Acth and Cortisone. The patients were divided into nine study groups, four of these groups comprised patients experiencing initial attacks. Of these four one was made up of children ill for fourteen days or less, one of children ill for fifteen or more days, one of adults ill for fourteen days or less, and one of adults ill for fifteen days or more. Patients with recurrent attacks were assigned to one of these four groups. All patients with chorea were assigned to a separate group.

Of 97 patients 49 received intensive penicillin therapy for 42 days and 48 received none. All of the study population received acetyl salicylic acid for 14 days to control acute symptoms. At the end of six weeks both treated and control patients were given 1.2 million units of Benzathine penicillin every five weeks for one year.

During the first six weeks there were no significant differences in the clinical manifestations between the two groups. The over-all results of the present study tend to show that penicillin influences favorably the incidence of valvular heart disease without affecting acute phase manifestations. The degree of reduction of valvular disease was considered significant in patients with moderate or absent valvulitis at the time therapy was instituted. Of these patients without advanced valvular damage 52 per cent in the control group exhibited valvular disease one year later as compared to only 21% of those who received penicillin. This effect of penicillin on the cardiac status can be attributed to its antibacterial action, and consequently these results indicate that the streptococcus continues to participate in the rheumatic reaction, even after acute symptoms of the disease have disappeared.

It is suggested that although the streptococcus induces rheumatic fever and valvular lesions by the liberation of some unknown substance, a direct invasion of the valve may subsequently ensue. In this study Group A streptococci were isolated from the oropharynx in only 15 per cent of patients. However 79 per cent of all patients exhibited an elevated anti-streptolysin — a titre of at least over 250 units. This discrepancy may have been due to the fact that the organism was a non-beta-hemolytic streptococcus.

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*Goetz, F.C. and Egdahl, R.H., Fed. Proc. 17:55, 1958

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If these conclusions are valid, the employment of large doses of penicillin will prevent rheumatic valvulitis as well as the symptoms of acute rheumatic fever. However it is agreed that acetylsalicylic acid or one of the adrenocortical preparations be used in conjunction with penicillin until additional data is obtained to substantiate these results.

Monte Kowall.

◆

Thyroglobulin Antibodies in Multiple Thyroid Diseases: Blizzard, R. M., Hamwi, G. J., Skillman, T. G. and Wheeler, W. E. New Eng. J. Med., 260: 112, 1959.

Circulating thyroglobulin antibodies have been demonstrated in the serum of patients with Hashimoto's thyroiditis (struma lymphomatosa) and patients with spontaneous myxedema. This has led to the concept that autoimmunization to autogenously released thyroglobulin is a causative factor in these disorders. The authors, using the red-cell hemagglutination technic of Boyden and the agar-gel precipitation technic of Doniach, tested for thyroglobulin antibodies in the sera of 161 patients with known thyroid diseases and 219 normal controls. The tests were positive in less than 4 per cent of the controls and in 35 per cent of the group with thyroid disorders. The agar-gel technic appeared to be considerably less sensitive than the hemagglutination method. Positive tests were demonstrated most frequently in patients with Hasimoto's disease and spontaneous myxedema, but a significant percentage of patients with thyrotoxicosis and patients with nontoxic nodular goiter also had circulating thyroglobulin antibodies. A high prevalence of penicillin hypersensitivity according to past history was obtained in the patients demonstrating the thyroglobulin antibodies. The authors concluded that their data were supportive of the hypothesis that autodestruction is an etiologic factor in Hashimoto's disease and spontaneous myxedema, and plays a role in the control of thyrotoxicosis.

G. A. Lillington.

◆

The Early Diagnosis of Portal Hypertension: Berci, G., Foldes, G., Herczeg, T. and Lehoczky, D. M. J. Australia, 45: 319, Sept., 1958.

It is desirable to recognize the stage when chronic hepatitis turns into cirrhosis. It may well be that the first evidence of the transition will be a rise in portal venous pressure. The "free hepatic vein pressure" obtained by hepatic vein catheterization, is generally agreed to be identical with the portal vein pressure. Fourteen patients had this examination performed. The authors consider 143 mm. of water to be the upper limit of pressure in the closed hepatic vein of normal subjects. It is felt that the pressure in the hepatic vein is more reliable as an indicator of the degree of intrahepatic vascular resistance than are indirect methods.

The potential field of inquiry which is opened by this method of measuring hepatic vein pressure is very considerable, and further studies of this nature should give us a much better understanding of the haemodynamics of the portal circulation in health and in disease.

A. Rogers.

◆

"A Comparison Between Radiology and Oesophagoscopy in the Investigation of Reflux Oesophagitis." Martin-Spiro. British Journal of Radiology, Vol. XXXI, No. 371, November, 1958.

It is in relatively recent years only, that reflux oesophagitis has been recognized as a clinical entity despite the fact that it is a fairly common ailment.

Clinically it is characterized by a painful burning sensation behind the sternum or in the epigastrium, often brought on by stooping or lying down. The pain may radiate into the chest and neck and down one or both arms and hence may simulate angina.

The author studied 100 cases of reflux oesophagitis which were diagnosed on clinical grounds. All cases were examined radiologically and 65 of these were oesophagoscoped. The radiological assessment of the condition of the oesophageal mucosa was considered to be unreliable and an x-ray diagnosis of oesophagitis was made in only 12 of the 65 cases oesophagoscoped whereas, a positive diagnosis was possible by oesophagoscopy in all 65 cases.

However, x-ray examination revealed the presence of an associated hiatus hernia in almost 90% of all cases and gastro-oesophageal reflux due to incompetence of the sphincteric mechanism in 70% of cases.

Stenosis complicating oesophagitis was detected radiologically in 27%.

By comparison Oesophagoscopy was not nearly so reliable in the diagnosis of these associated conditions.

The two methods of investigation revealed a peptic ulcer in the lower oesophagus with approximately the same degree of frequency. Ulceration of the mucosa was detected in a total of 14 cases only out of the 65 who were subjected to both diagnostic procedures.

The author points out that gastro-oesophageal reflux was in some cases an intermittent phenomenon which may be apparent at the initial exami-examination and not at a second examination and vice versa. This has probably been the experience of the majority or radiologists.

J. P. MacLaughlin.

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Book Reviews

The Medical Annual — 1958. Seventy-sixth issue. The MacMillan Co. of Canada Ltd. 579 pp. Price $7.50.

The 76th consecutive issue of the Medical Annual has recently appeared on the shelves of the library. Published by the MacMillan Company of Canada and edited by Sir Henry Tidy and R. Milner Waller, the present edition of 579 pages provides a very complete review of important medical writings of the years 1956 and 1957.

The subject matter of the book has been divided into a number of subsections ranging from child psychiatry to blood disorders to orthopedic and traumatic surgery. Each subsection has been written by a specialist in the field; in most cases from the United Kingdom. A section on recent pharmaceutical preparations at the end of the edition is of little value to the Canadian reader. Several special articles have been added to the 1958 volume and are excellent. The discussion of the complex subject of Intersexuality by P. M. F. Bishop is a notable high-light of this volume. A timely discussion of the Danger Arising from the Medical Use of X-rays by J. H. Middlemiss emphasizes the cumulative risk accompanying exposure to ionizing radiation.

It is difficult to be highly critical of the 76th edition of the Medical Annual as it very briefly and concisely covers the important advances made in many of the subspecialties in medicine in 1956 and 1957. Both the general practitioner and specialist will benefit from reading the 1958 Medical Annual.

P.A.G.

♦

Treatment in Internal Medicine: Harold Hyman, M.D., pp. 609. J. B. Lippincott Company, Philadelphia, Montreal.

The publishers introduce this book as "an authoritative compendium of current treatment procedures outstanding for its explicit presentation of technical knowledge and its combination of wisdom and common sense." Walter C. Alvarez, describes it as a book "well organized, well written and attractively printed." The author calls it a "functional" text.

This reviewer regrets that he is unable to join in the chorus of praise. Conceding that the book is attractively printed and well indexed, he remains blind to its other alleged virtues. He is unable to see any "common sense" in treating angina pectoris with oxygen (page 311), or the "less understanding" hypertensive with a "course of shots (i.e., vitamins, cacodylate of soda, etc.)" (page 357), or cerebral thrombosis with stellate block (page 330). Nor can he discern any trace of "wisdom" in a ponderous pronouncement such as the following: "a common cause of error in prognosis is failure to recognize that patients rarely die of organic disease. They usually succumb to a breakdown of a physiologic mechanism that is often immeasurable" (page 581).

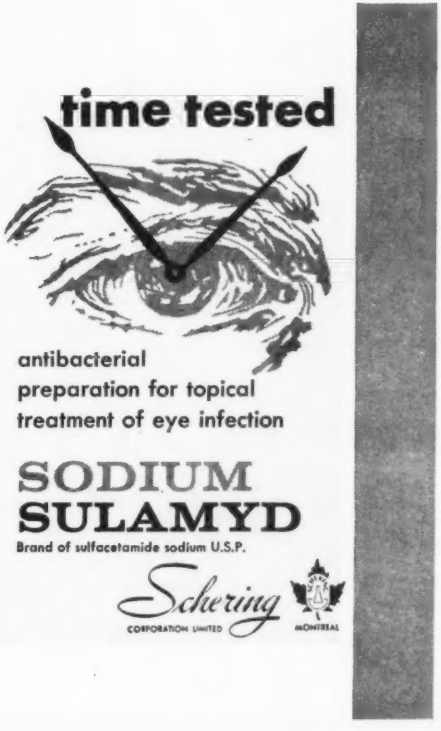
Ready to overlook such gross mis-statements as "regard osteoporosis as a symptomatic condition resulting from decalcification" (page 550), the reviewer is reluctant to close his eyes to the inadequacies of information and guidance in the management of emergencies, esp. diabetic coma.

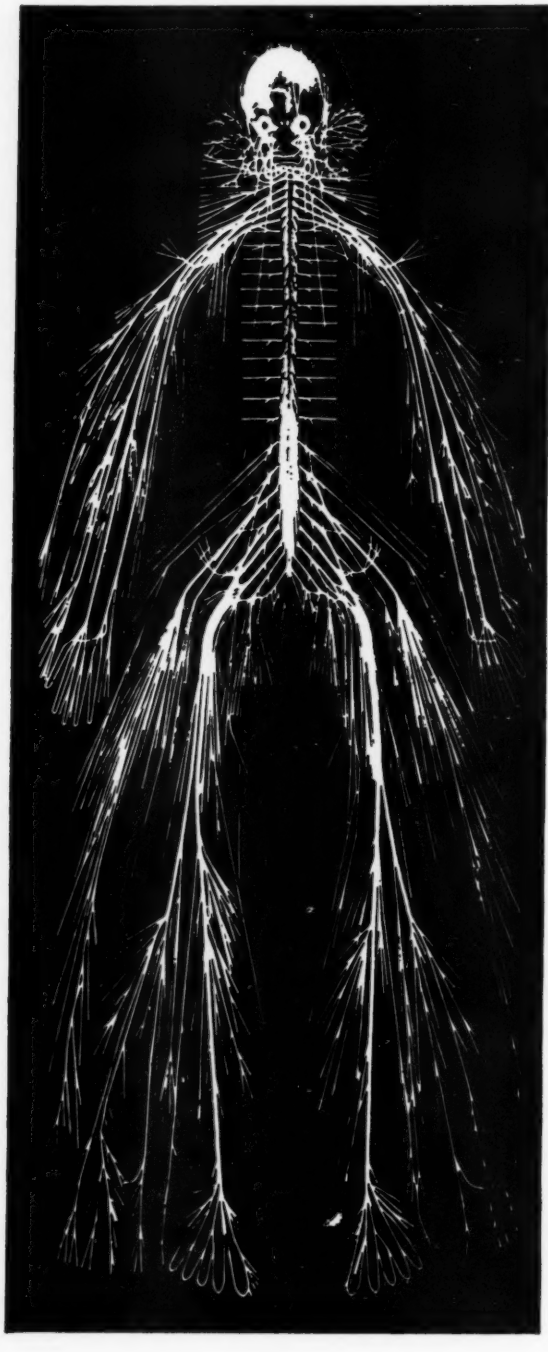
This reviewer is also unwilling to applaud the abundance of pompous terms — allergenicities "spasmosis," "characterologic" — and the redundance of a style that is both pretentious and pontifical.

The publishers recommend this book as a "guide to the best that modern medicine has to offer in therapy." This may be so. A guide to the best, however, is not necessarily a best guide.

S.V.

♦





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←Dissection of nervous system by R. B. Weaver, A.M., M.D., Sc.D., late Professor of Anatomy, Hahnemann Medical College and Hospital. Courtesy of Hahnemann Medical College Museum.

Social News

Reported by K. Borthwick-Leslie, M.D.

Having survived a three weeks tour of Montreal, blizzard-bound, French drivers and **taxi** drivers (one gloriously singing happy, slithering around Mount Royal on an ice-bound night, whipping through "Stop - Arretez" signs—picks up a jug and gurgles down a lusty slug right smack in the face of ye motor cycle cop — and merrily on our way. Thank Heavens for the old Presbyterian upbringing of "what is to be, will be"! Before I finally reached my destination though, I was almost reduced to grabbing said jug and gurgling a lusty slug too — my shattered nerves — (more shattered at a $11.78 fee) — oh well, wrong profession. Also survived the wedding and showers, etc. Love that gal — and I think have persuaded the parents, etc. that in the West, "Tug Boat Annie" has her moments of not broncho busting, but being a sedate Christian-like lady, kind hearted too, if holding up the wedding ceremony fifteen minutes due to those . . . transportation facilities.

Anyway, have also survived wading through three weeks of newspapers for news, so if you or yours are neglected, please envision yourselves wading through three weeks of Tribune, Press, Alumni and other journals and say "God help Katie."

From the East — Harold and Pat Blondal say "Hello" to all their friends and associates. Both love Montreal. Harold is steamed up with his work and continued research work, and Pat, as all of us, thrilled at having her first novel published — serial rights by Chatelaine starting in September. Congratulations? You bet!

♦

I have been chastised by ye editor because of words of omission — to Dr. Gellman, recently attached to Winnipeg Clinic, I'm not sure whether to apologize for my gremlins or not.

In correction of the February issue the notice should have been:

"The Winnipeg Clinic announce that David D. Gellman, M.D., M.B., B.S., M.R.C.P. (Lond.) and Glen A. Lillington, B.Sc., M.D. (Man.), M.S. (the latter recently associated with the Mayo Clinic) have joined the Dept. of Internal Medicine." My error — rather expected that with all those overseas degrees my public would realize the "latter" would apply to Dr. Lillington. Sorry, or am I?

♦

Congratulations to Dr. Matthew K. Kiernan, F.A.C.R. who on February 6, 1959 in Chicago, at convocation ceremonies following the regular meeting of the American College of Radiology, received his Fellowship in the American College of Radiology." Nice going, Matt.

Dr. Norman C. Hill, M.D. '52, M.Sc. '54, having completed his fellowship in neurological survey at the Mayo Foundation, Rochester, Minn., has been awarded the American Academy of Neurological Surgery prize for his work: "Cerebrospinal Fluid Proteins, Glycoproteins and Lipoproteins in obstructive lesions of the Central Nervous System."

♦

More very welcome financial support for Research has been announced. $9,640 from the Muscular Dystrophy Association for pharmacological work under Dr. G. B. Frank, from the Imperial Oil Co. $3,500 in Chemistry, conducted by Prof. B. L. Funt, and from Ayerst, McKenna and Harrison Ltd. towards pharmacological research, by Dr. Mark Nickerson.

♦

Dr. and Mrs. F. M. Brunheimer, in Chicago, announce the birth of Kristin Joanna, Jan. 29, 1959.

♦

Drs. Michael and Joyce (nee Findlay) Grace, of Transcona, welcome Elizabeth Mary, baby sister for Michael Patrick and Catherine, Feb. 3, 1959.

♦

Dr. and Mrs. C. Lavoie proudly announce the arrival of their third son, Richard Joseph, January 31, 1959.

♦

Dr. and Mrs. C. A. Young welcomed Elizabeth Louise on February 11, 1959.

♦

Dr. and Mrs. K. D. McKenzie also proudly announce the birth of Elizabeth Lynn, as of February 21, 1959.

♦

Dr. and Mrs. R. E. Jordan, also a daughter, Anne Wilona, on Feb. 22, 1959, sister for John and David.

♦

Born to Dr. and Mrs. Earl Hershfield on Feb. 1, 1959, a son — also the first grandchild for Dr. C. S. Hershfield.

♦

Dr. and Mrs. T. K. Goodhand welcome their son John Bruce on Feb. 9, 1959 — a brother for Joyce, Lois and Margo.

♦

Dr. and Mrs. Ian M. Laing welcome a daughter, Margo Allison on Feb. 20, 1959—sister for Elizabeth and Ross.

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Available in 15 cc. plastic squeeze bottles that deliver either spray or drops.

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MONTREAL CANADA

Brandon and District Medical Association

January 21, 1959

A reception was held at the home of the Medical Superintendent. Following this a dinner was served in the nurses' residence of the hospital, presided over by the Medical Superintendent.

Dr. Stuart Schultz welcomed all guests, including the special guests, Dr. Edward Johnson, President of the Manitoba Medical Association, and Mrs. Johnson, of Selkirk, Dr. M. T. Macfarland, Executive Director of the Manitoba Medical Association, and Mrs. Macfarland, Dr. J. D. Adamson, Dr. Norman C. Hill, Dr. and Mrs. E. L. Ross and Dr. H. M. McIntyre, all of Winnipeg.

The following physicians of Brandon were present: Drs. E. M. Bristow, D. G. Coghlin, R. P. Cromarty, A. Elliott, H. S. Evans, J. Fang, J. A. Findlay, F. Fjeldsted, N. Y. Youbert, A. C. Klassen, M. Kozakiewicz, A. P. Lapko, J. M. Matheson, S. Murphy, R. F. M. Myers, P. F. Payne, A. H. Povah, J. E. Rowlands, W. Schlichther, J. H. Scott, V. Sharpe, W. Shaharow, E. J. Skafel, R. H. D. Sykes, D. Verinder; W. Nakielny, Rivers; W. H. Patterson, Carberry; G. T. McNeill, Carberry; R. A. Christie, Neepawa; R. O. Hinch, Minnedosa; J. D. McMillan, Oak River; A. L. Paine, Ninette; J. A. Jemson, Dunrea; W. K. Hames, Kenton; M. Scherz, Oak Lake; M. A. Sirett, Erickson; H. C. Stevenson, Minnedosa.

The senior staff of the Brandon Mental Hospital were also present.

Dr. Paul Hirsch presided over the scientific session which was held in the Lecture Theatre. Dr. Norman C. Hill gave a paper on "Medical and Surgical Aspects of Cerebral Vascular Disease." This created considerable interest, judging by the number of questions following Dr. Hill's fine presentation. The second paper was "The Use of Tranquilizers in General Practice," prepared by Dr. Schlichther and Dr. Payne of the Hospital Staff, and read by Dr. Payne. This was a valuable paper as Tranquilizers at the present time are in very wide use.

The ladies attended a dinner, and following this were entertained by Mr. Lubor Zink, editorial writer of the Brandon Sun. Mr. Zink has had a very interesting career as a member of the Czech Foreign Office and the British Broadcasting Corporation. He presented a number of beautiful slides of France, Italy, and other countries of Europe, and at the same time provided interesting commentary on the many centres of historical interest.

The next Scientific Session of the Brandon Mental Hospital Staff will be held about the middle of February.

S. S.

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hyperacidity

Gelusil

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fast, lasting relief
no acid rebound
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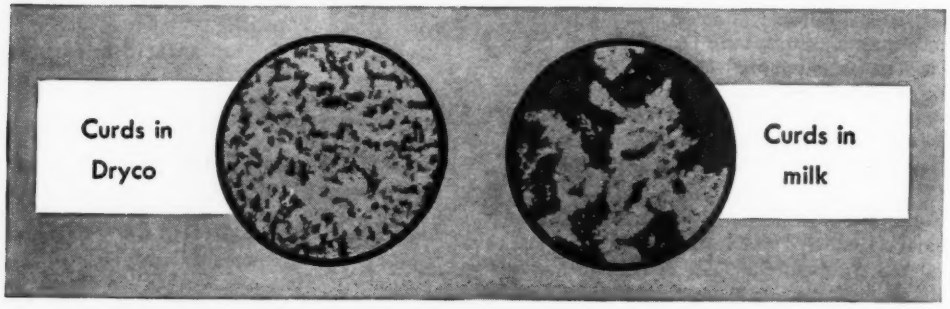

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Future Events

The Annual Meeting and Scientific Convention of the Manitoba Chapter of the College of General Practice of Canada will be held at Clear Lake, Manitoba on May 31st, June 1st and 2nd, 1959.

♦

The Third Annual Post-Graduate Course in Fractures and Other Trauma will be presented by the Chicago Committee on Trauma of the American College of Surgeons from Wednesday, April 15, through Saturday noon, April 18, 1959, at the John B. Murphy Memorial Auditorium, 50 East Erie Street, Chicago 11, Illinois.

♦

The 24th Annual Congress of the North American Federation, International College of Surgeons, will be held in Chicago, September 13-17, 1959. The federation is composed of the United States, Canadian, Mexican and Central American Sections. For information, write to the Secretariat, International College of Surgeons, 1516 Lake Shore Drive, Chicago 10, Ill.

The Summer School of Alcohol Studies of the Laboratory of Applied Biodynamics, Yale University, New Haven, Connecticut, will hold its seventeenth annual session in 1959 during the 4-week period June 28-July 23 inclusive.

♦

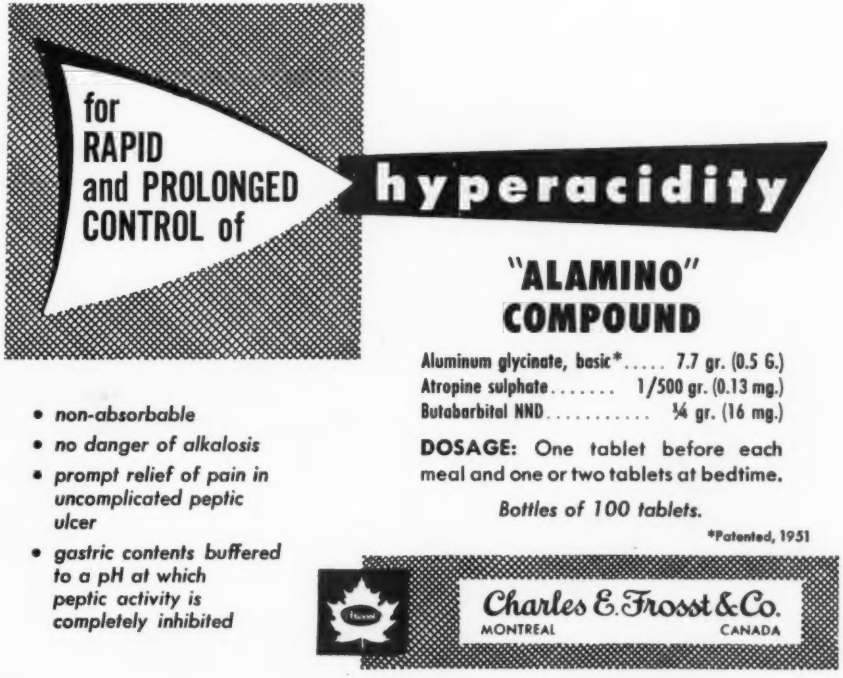
The 12th biennial International Congress of the International College of Surgeons will be held in Rome, Italy, May 15-18, 1960. For information write to the Secretariat, International College of Surgeons, 1516 Lake Shore Drive, Chicago 10, Ill.

♦

The annual spring meeting of the New York Surgical Division, International College of Surgeons, will be held at the Concord Hotel, Kiamesha Lake, N.Y., May 28-30, 1959. For information, write to Dr. Wilton S. Weinberg, chairman of arrangements, 37-41, 75 Street, Jackson Heights, 72, N.Y.

♦

The first Canadian Symposium on Non-Gonococcal Urethritis and Human Trichomoniasis, to be held on September 21 and 22, 1959, at the Notre-Dame Hospital, 1560 Sherbrooke St. East, Montreal.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Aluminum glycinate, basic*..... 7.7 gr. (0.5 G.)
Atropine sulphate..... 1/500 gr. (0.13 mg.)
Butabarbital NND..... ¼ gr. (16 mg.)
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Bottles of 100 tablets.
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THROUGH THE DAY
AND
THROUGH THE NIGHT

HOSPITAL MEETINGS

Hospital	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday
Children's	10:30 Staff Rounds "A" Service 12:00 Surgical Rounds	10:00 Staff Rounds "B" Service	9:30 Staff Rounds "C" Service 11:00 Clinical Path. Conference 11:00 Death Review (4th Wednesday)	11:00 Grand Ward Rounds	12:30 Clinical Luncheon (1st Friday)	9:30 Newborn Conference
Deer Lodge	Clinical Luncheon (1st Monday)			11:00 Ward Rounds		
Grace		Clinical Luncheon (3rd Tuesday)	9:00 Paediatrics 9:45 Medicine 10:30 Ob. & Gyn. 11:15 Surgery	12:00 - 2:00 p.m. Weekly Seminar		
Misericordia	Tissue Committee (3rd Monday)	Clinical Luncheon (2nd Tuesday)				8:30-12:30 Ward Rounds
Municipal			7:30 p.m. Review of Deaths (2nd Wednesday)			8:30 Clinical Staff Conf. and Ward Rounds
St. Boniface	9:00 Paediatric Rounds	11:00 Surgical Rounds	9:00 Obstetrical 11:00 Grand Rounds 12:30 Cardiac Unit (4th Wednesday)	11:00 Tumor Clinic 12:00 Clinical Luncheon (2nd & 4th Thurs. ex. July & Aug.)		
St. Boniface Sanatorium	12:30 Clinical Luncheon (1st or 2nd Monday)					
Victoria					Clinical Luncheon (3rd Friday)	
Winnipeg General		11-12:00 Medical Ward Rounds	9-10:00 Tumor Clinic 10-11:00 Surgical	12:15 Clin. Lunch. (1st & 3rd Thurs.)		
Brandon General			Medical Staff Lunch (Wed. prior to 2nd Tues. each month)			10:00-noon Clinical Drs. from S.W. Manitoba invited (Nov. to May)

Report of 273 treated cases of skin and soft tissue infections documented by Canadian Investigators

Signemycin

TETRACYCLINE-OLEANDOMYCIN

In this particular study, Signemycin proved successful in 95.7% of the cases and side effects were observed in only 8.4%. These reactions were primarily mild diarrhea and in no instance caused discontinuance of therapy

Response to Signemycin

INFECTION	TOTAL	SUCCESSFUL	UNSUCCESSFUL
Abscess, genera	36	33	3
Abscess, gluteal	2	2	—
Abscess, perianal	3	3	—
Acne	22	20	2
Boils	30	30	—
Carbuncles	10	10	—
Cellulitis	26	26	—
Dermatitis	4	3	1
Erysipelas	1	1	—
Folliculitis	4	4	—
Furunculosis	69	66	3
Hydradenitis	2	2	—
Impetigo	8	8	—
Lacerations, wounds (infected)	17	17	—
Lymphadenitis	5	5	—
Paronychia	2	2	—
Ulcers, infected	4	3	1
Mastitis	21	21	—
Unspecified	7	5	2
	273	261	12

Case No. 260: A 27 year old mechanic suffered from acute furunculosis due to Staphylococcus aureus, found to be resistant to all antibiotics but oleandomycin. Previous therapy with penicillin, tetracycline and chloramphenicol had been unsuccessful. The patient was given 250 mg. Signemycin 4 times daily for 4 days. The infections responded excellently to this treatment. The patient developed eructations probably due to a duodenal ulcer but untoward effects caused by Signemycin were not observed.

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100 mg. capsules, bottles of 25 and 100 250 mg. capsules, bottles of 16 and 100	10 cc. bottles (5 mg./drop)	60 cc. bottles (125 mg. 5 cc.)	250 mg. and 500 mg. vials

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to prevent attacks

Peritrate 20 mg.

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Peritrate 20 mg. for routine prophylaxis to prevent attacks of angina pectoris; in the management of coronary insufficiency, and the postcoronary patient.

in angina pectoris

to relieve the acute attack

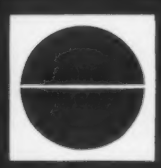
Sublingual

Peritrate with Nitroglycerin

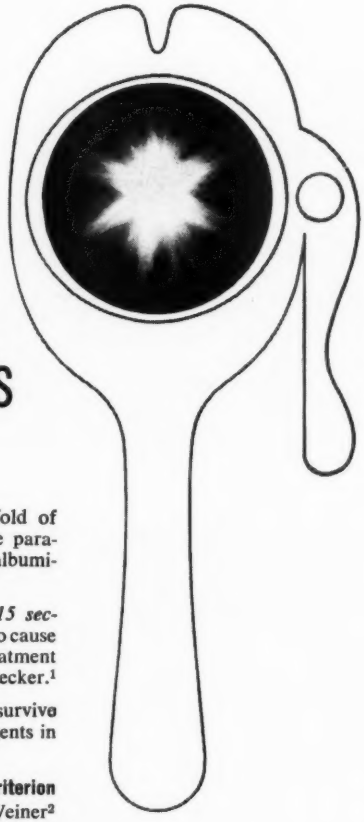
Replaces supplementary nitroglycerin in the Peritrate patient

Sublingual Peritrate with Nitroglycerin is a companion product to regular Peritrate. It replaces nitroglycerin — not Peritrate. It not only relieves the acute attack — it automatically supplies additional Peritrate for increased protection during the stress period. Peritrate with Nitroglycerin replaces nitroglycerin in any strength because the sublingual Peritrate increases the immediate nitrate level.

Help your anginal patients lead a more normal life by prescribing Peritrate 20 mg. q.i.d. *and* Peritrate (10 mg.) with Nitroglycerin (1/200 gr.) p.r.n.



97% clinical success following **explosion** of trichomonads



VAGISEC* *liquid and jelly*

PURSUE trichomonads into every fold of vaginal mucosa – reaching even those parasites buried under thick, tenacious albuminous secretions.

EXPLODE all trichomonads *within 15 seconds of contact!* No flagellate remains to cause troublesome flare-ups. Successful treatment in 97% of patients is reported by Decker.[1]

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Repeated negative cultures—strictest criterion
Using cultures, the most critical test, Weiner[2] reported 46 of 51 patients "cured" by VAGISEC therapy. 'Round-the-clock therapy – vaginal scrub with VAGISEC liquid in the office and instillation of VAGISEC jelly, followed by home douches and jelly—ensures eradication of organisms. Annoying symptoms (leukorrhea, pruritus, burning) often disappear after the first treatment.[1] Three to four weeks of therapy usually are sufficient for most cases.[1-3]

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References: 1. Decker, A.: New York J. Med. *57*:2237 (July 1) 1957.
2. Weiner, H. H.: Clin. Med. *5*:25 (Jan.) 1958.
3. Davis, C. H.: West. J. Surg. *63*:53 (Feb.) 1955.

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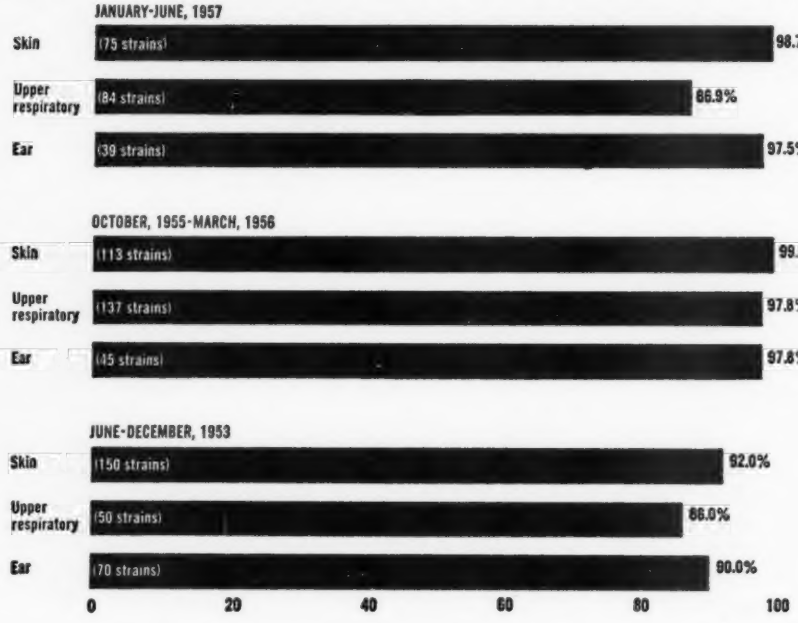

*Adapted from Royer, A., in Welch, H., & Martí-Ibañez, F.: Antibiotics Annual 1957-1958, New York, Medical Encyclopedia, Inc., 1958, p. 783.

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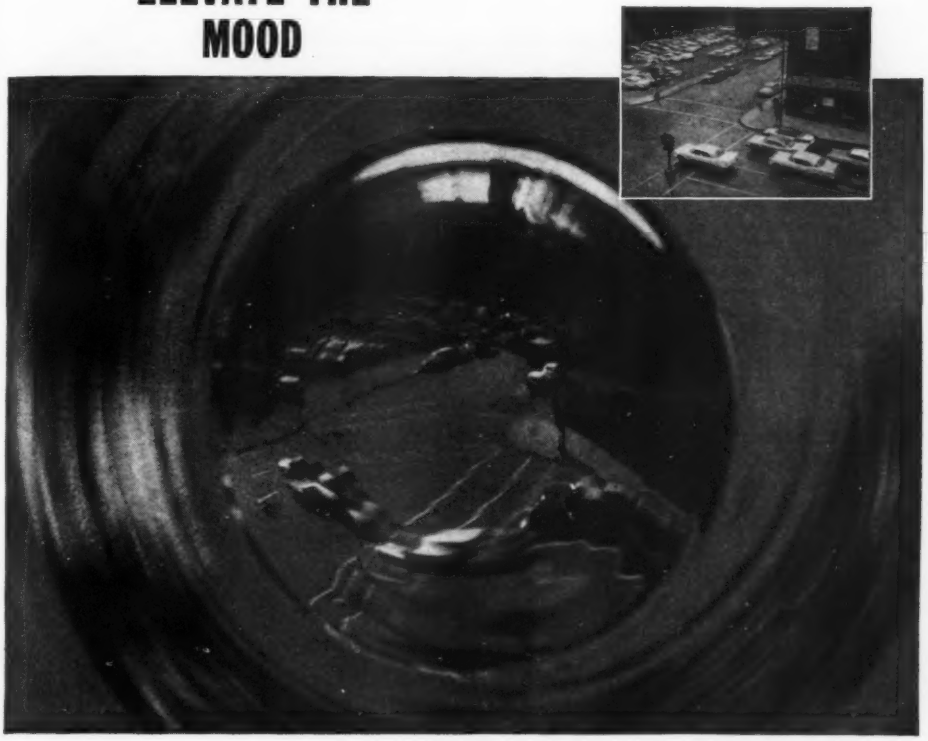

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*Pratt, R. T. C., and McKenzie, W.: Anxiety States Following Vestibular Disorders, Lancet *2*:347 (Aug. 16) 1958.

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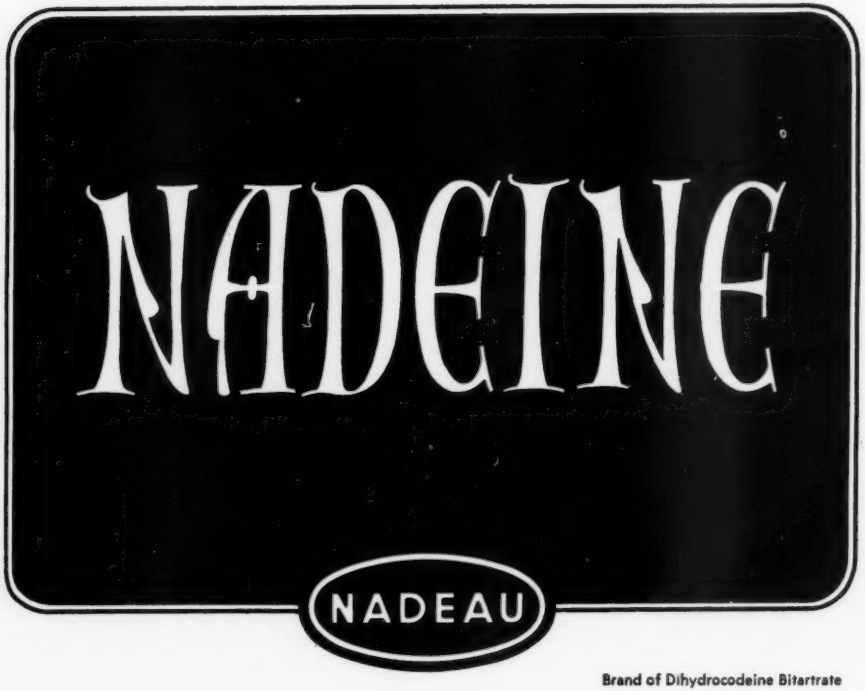

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For the relief of pain after surgery, following trauma, pain associated with malignancy, as a supplement to anesthetics.

A valuable analgesic during labor because it does not depress the fetal respiratory mechanism.

ITS MAIN FEATURE IS LITTLE OR NO RESPIRATORY DEPRESSION and generally an absence of nausea or other ill effects.

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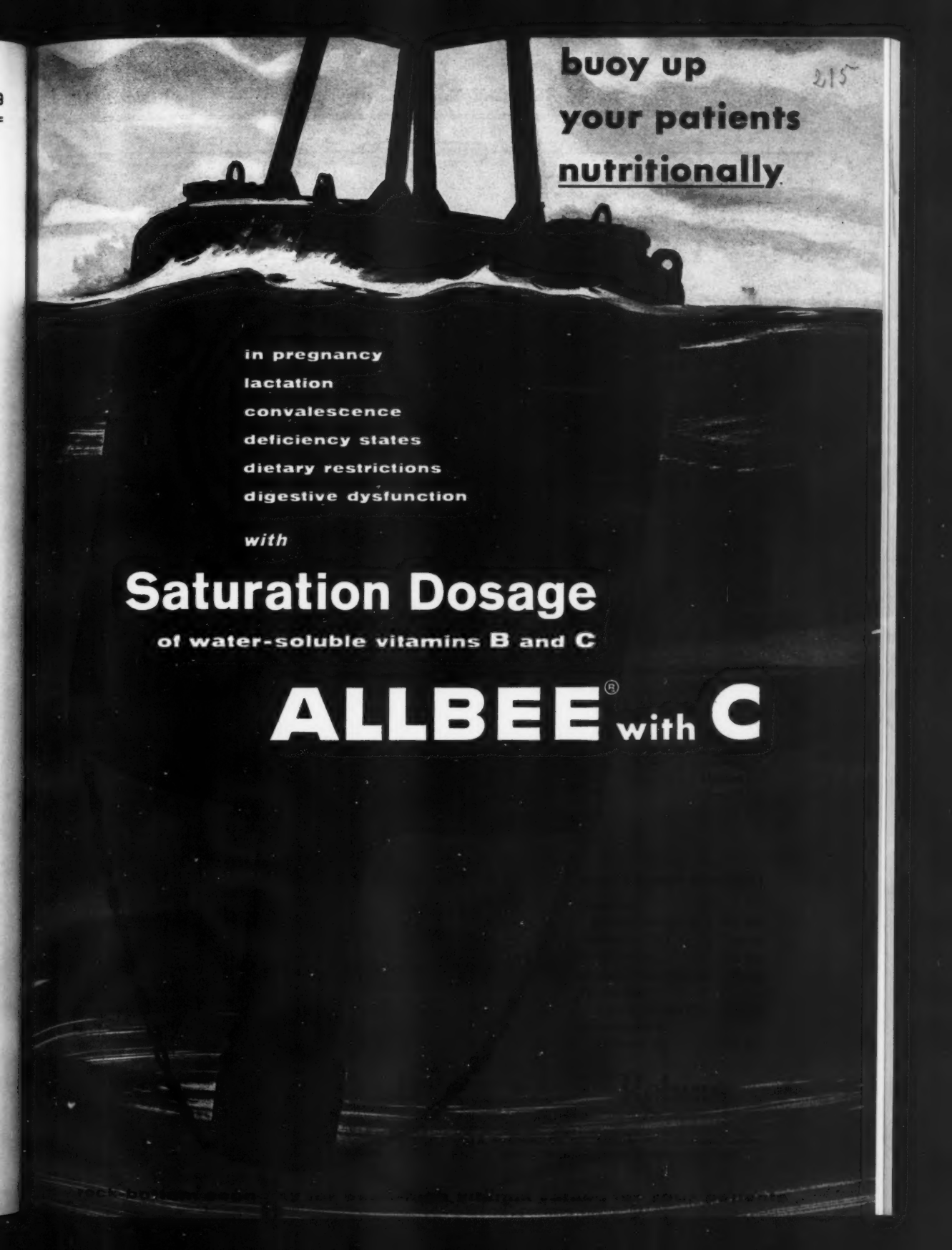
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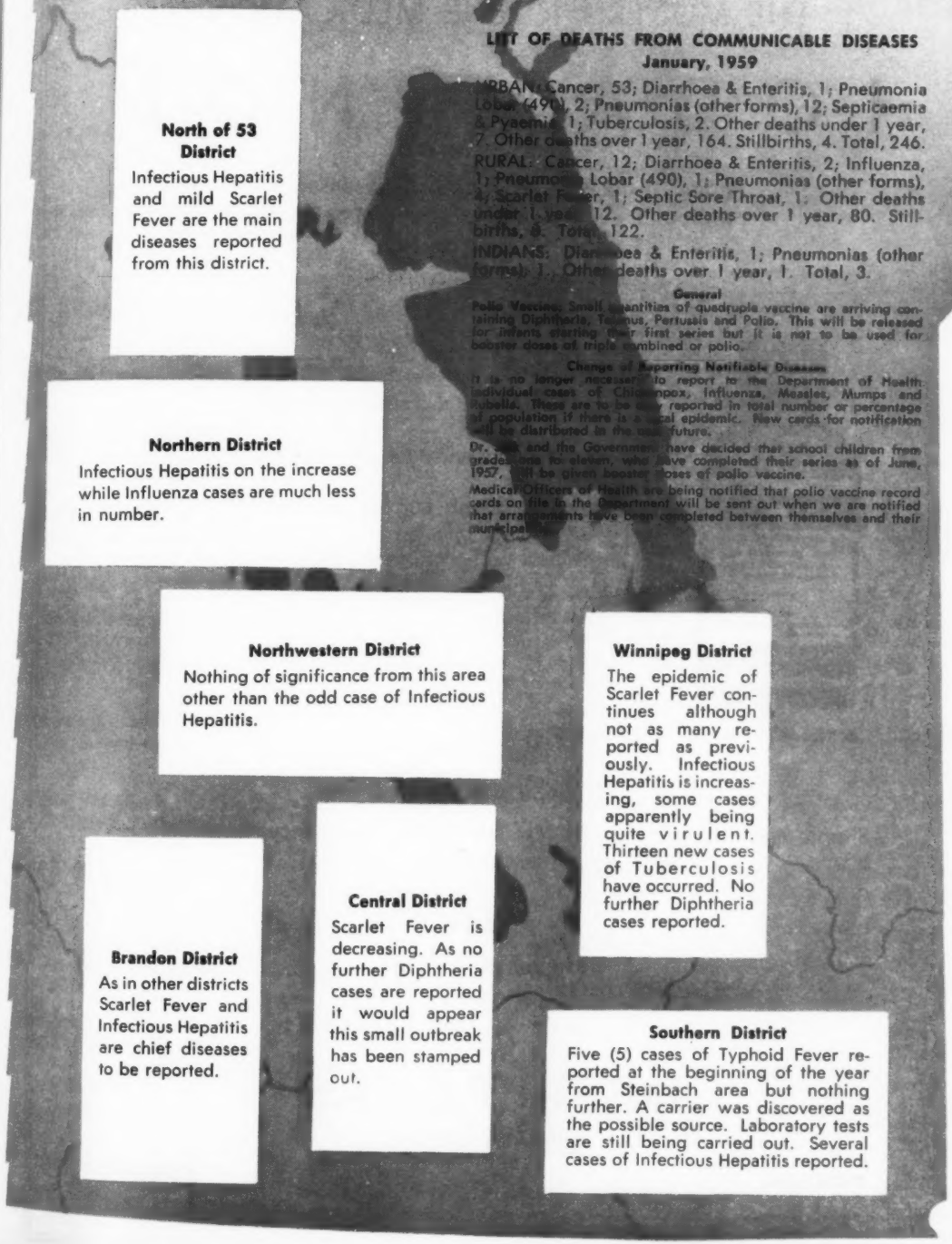
DEPARTMENT OF HEALTH & PUBLIC WELFARE

COMMUNICABLE DISEASE PICTURE



North of 53 District

Infectious Hepatitis and mild Scarlet Fever are the main diseases reported from this district.

Northern District

Infectious Hepatitis on the increase while Influenza cases are much less in number.

Northwestern District

Nothing of significance from this area other than the odd case of Infectious Hepatitis.

Brandon District

As in other districts Scarlet Fever and Infectious Hepatitis are chief diseases to be reported.

Central District

Scarlet Fever is decreasing. As no further Diphtheria cases are reported it would appear this small outbreak has been stamped out.

Winnipeg District

The epidemic of Scarlet Fever continues although not as many reported as previously. Infectious Hepatitis is increasing, some cases apparently being quite virulent. Thirteen new cases of Tuberculosis have occurred. No further Diphtheria cases reported.

Southern District

Five (5) cases of Typhoid Fever reported at the beginning of the year from Steinbach area but nothing further. A carrier was discovered as the possible source. Laboratory tests are still being carried out. Several cases of Infectious Hepatitis reported.

LIST OF DEATHS FROM COMMUNICABLE DISEASES
January, 1959

URBAN: Cancer, 53; Diarrhoea & Enteritis, 1; Pneumonia Lobar (490), 2; Pneumonias (other forms), 12; Septicaemia & Pyaemia, 1; Tuberculosis, 2. Other deaths under 1 year, 7. Other deaths over 1 year, 164. Stillbirths, 4. Total, 246.

RURAL: Cancer, 12; Diarrhoea & Enteritis, 2; Influenza, 1; Pneumonia Lobar (490), 1; Pneumonias (other forms), 4; Scarlet Fever, 1; Septic Sore Throat, 1. Other deaths under 1 year, 12. Other deaths over 1 year, 80. Stillbirths, 8. Total, 122.

INDIANS: Diarrhoea & Enteritis, 1; Pneumonias (other forms), 1. Other deaths over 1 year, 1. Total, 3.

General

Polio Vaccine: Small quantities of quadruple vaccine are arriving containing Diphtheria, Tetanus, Pertussis and Polio. This will be released for infants starting their first series but it is not to be used for booster doses of triple combined or polio.

Change of Reporting Notifiable Diseases

It is no longer necessary to report to the Department of Health individual cases of Chickenpox, Influenza, Measles, Mumps and Rubella. These are to be only reported in total number or percentage of population if there is a local epidemic. New cards for notification will be distributed in the near future.

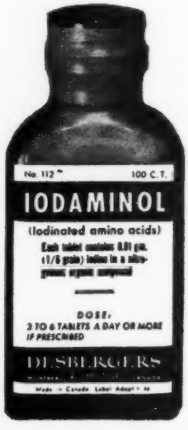
Dr. [illegible] and the Government have decided that school children from grades one to eleven, who have completed their series as of June, 1957, will be given booster doses of polio vaccine.

Medical Officers of Health are being notified that polio vaccine record cards on file in the Department will be sent out when we are notified that arrangements have been completed between themselves and their municipal [illegible]

THE MODERN IODINE MEDICATION

IODAMINOL

Iodine - Amino Acids permit high dosages without the untoward effects common to iodides, Lugol's solution, iodo-proteins, iodo-lipids



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Each IODAMINOL tablet contains 1/6 grain Iodine (the equivalent of 4 drops of fresh Lugol's solution) combined with Amino Acids.

INDICATIONS:

Simple and Exophthalmic Goiter; Toxemia of Pregnancy; Rheumatism; Septicemia; Arteriosclerosis; Tonsilitis.

DOSAGE:

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MONTREAL CANADA

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G. J. Bowen ..... GR 5-4559
R. G. (Bud) Harman ..... LE 3-7509
Alan (Al) M. Grant ..... AL 6-0125
Bruce Hunter ..... GL 2-5263

Arlington-Funk Laboratories, division U.S. Vitamin Corp. of Canada, Ltd.
Ed Lessor ..... GL 3-0807

Ayerst McKenna and Harrison
W. R. Card ..... HU 9-7115
C. C. Savage ..... SU 3-4558
Jack Ostrow ..... ED 4-3240

Borden Company Ltd.
Ken Hodges ..... AL 3-4319

British Drug Houses
W. S. Langdon ..... GL 3-1325
H. Harvey ..... TU 8-5341

Ciba Company Ltd.
Edward Stephany ..... HU 9-7292
Leslie D. MacLean ..... CE 3-3240

Connaught Laboratories
Brathwaites Ltd. ..... WH 2-2635

Frosst, Charles E.
W. M. Lougheed ..... HU 9-3963
W. J. McGurran ..... AL 3-0722
E. R. Mitchell ..... HU 9-6164
R. P. Roberts ..... AL 3-4032

Hoffmann-La Roche Limited
Paul E. Prendergast ..... AL 3-1962
Wilf Baldwin ..... HU 9-8236

Horner, Frank W. Limited
Jos. Lavitt ..... JU 9-1691
Wes Reimer ..... SP 2-69581
Frank Lowe ..... VE 2-5821

Lederle Laboratories
J. G. Jonasson ..... SP 5-4862
W. C. Hall ..... HU 9-2207
J. E. Smith ..... AL 3-0437

Merck, Sharp and Dohme (Canada) Ltd.
W. G. Ball ..... GR 5-5702
Noel J. Pritchard ..... GL 2-6880
E. J. Strimbicki ..... AL 3-5767

McNeil Laboratories of Canada Ltd.
B. M. Coutts ..... JU 2-5920

Nadeau Laboratory Ltd.
Andrew Desender ..... CH 7-4909

Ortho Pharmaceutical Corp.
Don MacDonald ..... GL 3-4549

Parke Davis & Co.
L. W. Curry ..... HU 9-1138
B. S. Fleury ..... GL 3-7071
R. J. Robinson (Brandon) 92-288
J. B. Peters ..... VE 2-3862

Pfizer Canada
E. E. Conway ..... TU 8-1193
W. R. Mitchell ..... GL 3-6226
W. G. Johnston ..... TU 8-1391
Blake Johns ..... SP 5-1404

Robins (Canada) Ltd., A. H.
Harold Tetlock ..... SP 5-5624
Fred Gallinger ..... ED 4-1367

Schering Corp. Ltd.
Halsey Park ..... HU 9-4346
John D. Nicolson ..... LE 3-4447
Allan L. Segal ..... HU 9-7701

Schmid (Canada) Ltd., Julius
H. V. Walker ..... LE 3-8664

Searle & Co., G. D.
Harry Chambers ..... LE 3-6558

Squibb & Sons, E. R.
A. B. Shaen ..... GL 2-9859
M. G. Waddell ..... GR 5-1552

Warner-Chilcott Labs.
A. L. (Andy) Argue ..... TU 8-1619
Gordon Harrower ..... AL 3-4147

Will, Charles R.
A. C. Payne ..... VE 2-2055

Winthrop Laboratories
R. M. Kelly ..... Res. GR 5-6038
A. E. Pauwels ..... CE 3-2024

Wyeth & Brother, John
A. W. Cumming ..... HU 9-5694
Stuart Holmes ..... JU 9-4273